Welcome to STN International! Enter x:x

LOGINID:ssspta1201txs

PASSWORD:
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 NEWS  3  Apr 09  BEILSTEIN: Reload and Implementation of a New Subject Area
 NEWS  4  Apr 09  ZDB will be removed from STN
 NEWS  5  Apr 19  US Patent Applications available in IFICDB, IFIPAT, and IFIUDB
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 NEWS 13  Jul 22  USAN to be reloaded July 28, 2002;
                  saved answer sets no longer valid
 NEWS 14  Jul 29  Enhanced polymer searching in REGISTRY
 NEWS 15  Jul 30  NETFIRST to be removed from STN
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 NEWS 17  Aug 08  PHARMAMarketLetter(PHARMAML) - new on STN
 NEWS 18  Aug 08  NTIS has been reloaded and enhanced
 NEWS 19  Aug 19  Aquatic Toxicity Information Retrieval (AQUIRE)
                  now available on STN
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 NEWS 22  Aug 26  Sequence searching in REGISTRY enhanced
 NEWS 23  Sep 03  JAPIO has been reloaded and enhanced
 NEWS 24  Sep 16  Experimental properties added to the REGISTRY file
 NEWS 25  Sep 16  Indexing added to some pre-1967 records in CA/CAPLUS
 NEWS 26  Sep 16  CA Section Thesaurus available in CAPLUS and CA
 NEWS 27  Oct 01  CASREACT Enriched with Reactions from 1907 to 1985
 NEWS 28  Oct 21  EVENTLINE has been reloaded
 NEWS 29  Oct 24  BEILSTEIN adds new search fields
 NEWS 30  Oct 24  Nutraceuticals International (NUTRACEUT) now available on STN
 NEWS 31  Oct 25  MEDLINE SDI run of October 8, 2002
 NEWS 32  Nov 18  DKILIT has been renamed APOLLIT

 NEWS EXPRESS  October 14 CURRENT WINDOWS VERSION IS V6.01,
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 NEWS INTER    General Internet Information
 NEWS LOGIN    Welcome Banner and News Items
 NEWS PHONE    Direct Dial and Telecommunication Network Access to STN
 NEWS WWW      CAS World Wide Web Site (general information)
```

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  * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * * *


FILE 'HOME' ENTERED AT 18:07:15 ON 19 NOV 2002

=> file reg
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.21       0.21

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DICTIONARY FILE UPDATES:  18 NOV 2002  HIGHEST RN 473870-51-8

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  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available.  See HELP
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=>
Uploading 10021667.str

L1      STRUCTURE UPLOADED

=> s l1
SAMPLE SEARCH INITIATED 18:07:48 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -     993 TO ITERATE

100.0% PROCESSED     993 ITERATIONS                                 6 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:        17970 TO    21750
PROJECTED ANSWERS:               6 TO      266

L2            6 SEA SSS SAM L1

=> d scan

L2   6 ANSWERS   REGISTRY  COPYRIGHT 2002 ACS
IN   2H-1-Benzopyran-2-carboxylic acid, 6-acetyl-7-[[6-(4-acetyl-3-hydroxy-2-
     propylphenyl)hexyl]oxy]-3,4-dihydro- (9CI)
MF   C29 H36 O7
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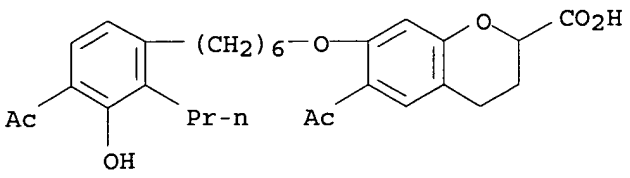
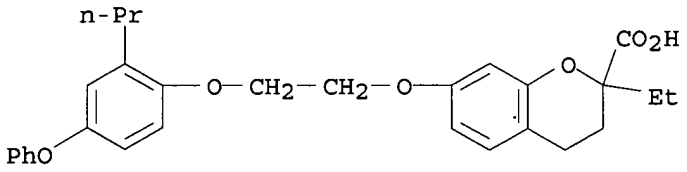


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

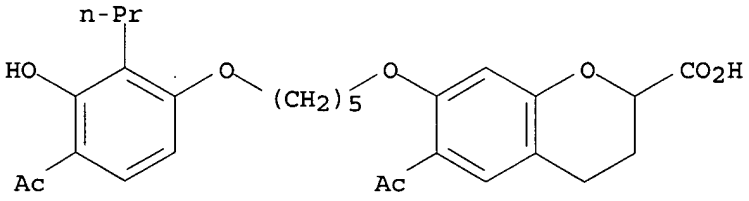
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):2

L2 6 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN 2H-1-Benzopyran-2-carboxylic acid, 2-ethyl-3,4-dihydro-7-[2-(4-phenoxy-2-propylphenoxy)ethoxy]- (9CI)
MF C29 H32 O6



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

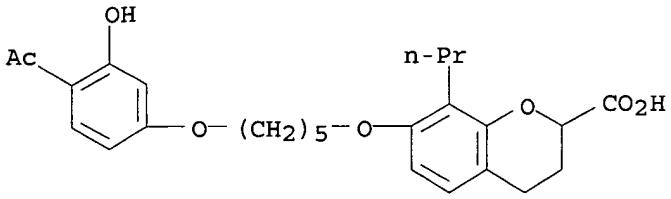
L2 6 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN 2H-1-Benzopyran-2-carboxylic acid, 6-acetyl-7-[[5-(4-acetyl-3-hydroxy-2-propylphenoxy)pentyl]oxy]-3,4-dihydro- (9CI)
MF C28 H34 O8
CI COM



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

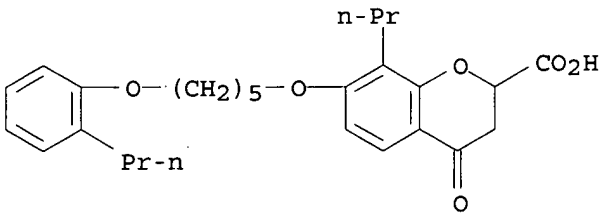
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):2

L2 6 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN 2H-1-Benzopyran-2-carboxylic acid, 7-[[5-(4-acetyl-3-hydroxyphenoxy)pentyl]oxy]-3,4-dihydro-8-propyl- (9CI)
MF C26 H32 O7



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

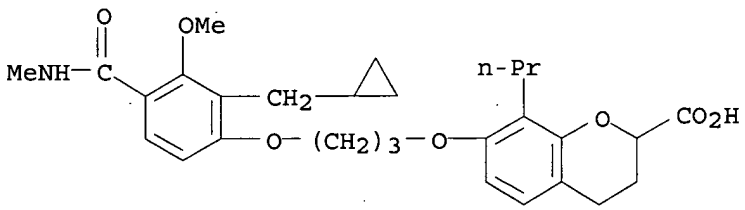
L2 6 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN 2H-1-Benzopyran-2-carboxylic acid, 3,4-dihydro-4-oxo-8-propyl-7-[[5-(2-propylphenoxy)pentyl]oxy]- (9CI)
MF C27 H34 O6



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):2

L2 6 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[2-(cyclopropylmethyl)-3-methoxy-4-[(methylamino)carbonyl]phenoxy]propoxy]-3,4-dihydro-8-propyl- (9CI)
MF C29 H37 N O7



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

ALL ANSWERS HAVE BEEN SCANNED

=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	1.90	2.11

STN INTERNATIONAL LOGOFF AT 18:10:23 ON 19 NOV 2002

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LOGINID:ssspta1201txs

PASSWORD:
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* * * * * * * * * * Welcome to STN International * * * * * * * * * *

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 NEWS 17  Aug 08  PHARMAMarketLetter(PHARMAML) - new on STN
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 NEWS LOGIN    Welcome Banner and News Items
 NEWS PHONE    Direct Dial and Telecommunication Network Access to STN
 NEWS WWW      CAS World Wide Web Site (general information)
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FILE 'HOME' ENTERED AT 18:12:15 ON 19 NOV 2002

=> file reg
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.21       0.21

FILE 'REGISTRY' ENTERED AT 18:12:28 ON 19 NOV 2002
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DICTIONARY FILE UPDATES:  18 NOV 2002  HIGHEST RN 473870-51-8

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Uploading 10021667.str

L1      STRUCTURE UPLOADED

=> s l1
SAMPLE SEARCH INITIATED 18:12:48 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -     96 TO ITERATE

100.0% PROCESSED      96 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:          1333 TO     2507
PROJECTED ANSWERS:                0 TO        0

L2            0 SEA SSS SAM L1

=> s l1 ful
FULL SEARCH INITIATED 18:12:58 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -   1431 TO ITERATE

100.0% PROCESSED    1431 ITERATIONS                              0 ANSWERS
SEARCH TIME: 00.00.04

L3            0 SEA SSS FUL L1
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=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	140.28	140.49

STN INTERNATIONAL LOGOFF AT 18:13:14 ON 19 NOV 2002

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LOGINID:ssspta1201txs

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2


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 NEWS 11  Jun 10  PCTFULL has been reloaded
 NEWS 12  Jul 02  FOREGE no longer contains STANDARDS file segment
 NEWS 13  Jul 22  USAN to be reloaded July 28, 2002;
                  saved answer sets no longer valid
 NEWS 14  Jul 29  Enhanced polymer searching in REGISTRY
 NEWS 15  Jul 30  NETFIRST to be removed from STN
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 NEWS 23  Sep 03  JAPIO has been reloaded and enhanced
 NEWS 24  Sep 16  Experimental properties added to the REGISTRY file
 NEWS 25  Sep 16  Indexing added to some pre-1967 records in CA/CAPLUS
 NEWS 26  Sep 16  CA Section Thesaurus available in CAPLUS and CA
 NEWS 27  Oct 01  CASREACT Enriched with Reactions from 1907 to 1985
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 NEWS 29  Oct 24  BEILSTEIN adds new search fields
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               AND CURRENT DISCOVER FILE IS DATED 01 OCTOBER 2002
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=> file reg
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.21       0.21

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DICTIONARY FILE UPDATES:  18 NOV 2002  HIGHEST RN 473870-51-8

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in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=>
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L1      STRUCTURE UPLOADED

=> s l1 ful
FULL SEARCH INITIATED 18:15:57 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -  19805 TO ITERATE

100.0% PROCESSED   19805 ITERATIONS                          155 ANSWERS
SEARCH TIME: 00.00.03

L2          155 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                       140.28     140.49

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FILE COVERS 1907 - 19 Nov 2002 VOL 137 ISS 21
FILE LAST UPDATED: 18 Nov 2002 (20021118/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

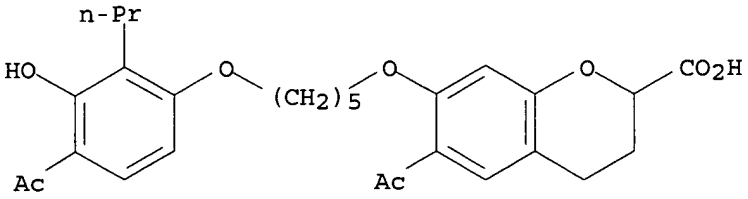
=> s l2
L3 101 L2

=> d l3 ibib hitstr abs 70-101

L3 ANSWER 70 OF 101 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:414418 CAPLUS
DOCUMENT NUMBER: 117:14418
TITLE: Antiallergic compositions containing platelet-activating factor antagonists and leukotriene D4 antagonists
INVENTOR(S): O'Donnell, Margaret; Welton, Ann
PATENT ASSIGNEE(S): Hoffmann-La Roche, F., A.-G., Switz.
SOURCE: Eur. Pat. Appl., 16 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 469477	A1	19920205	EP 1991-112577	19910726
EP 469477	B1	19950920		
R: AT, BE, CH, DE, DK, FR, GB, IT, LI, LU, NL, SE				
AT 128030	E	19951015	AT 1991-112577	19910726
CA 2048236	AA	19920203	CA 1991-2048236	19910731
ZA 9106036	A	19920527	ZA 1991-6036	19910731
AU 9181535	A1	19920213	AU 1991-81535	19910801
AU 651358	B2	19940721		
JP 04244028	A2	19920901	JP 1991-216009	19910801
US 5227378	A	19930713	US 1992-848564	19920309

PRIORITY APPLN. INFO.: US 1990-561743 19900802
IT **96566-25-5D**, mixts. with platelet-activating factor antagonists
140667-06-7
RL: BIOL (Biological study)
(antiallergic compns. contg.)
RN 96566-25-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 6-acetyl-7-[[5-(4-acetyl-3-hydroxy-2-propylphenoxy)pentyl]oxy]-3,4-dihydro- (9CI) (CA INDEX NAME)

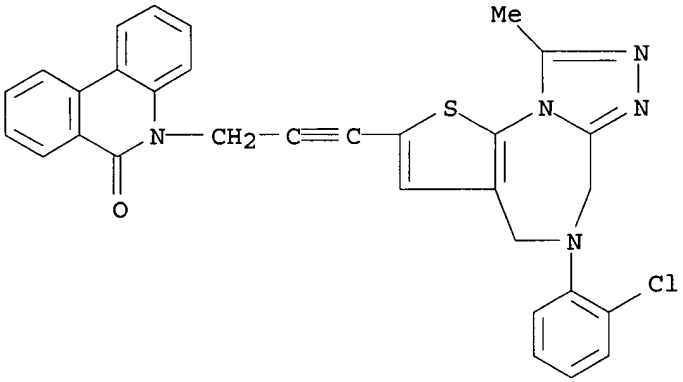


RN 140667-06-7 CAPLUS

CN 2H-1-Benzopyran-2-carboxylic acid, 6-acetyl-7-[[5-(4-acetyl-3-hydroxy-2-propylphenoxy)pentyl]oxy]-3,4-dihydro-, mixt. with 5-[3-[5-(2-chlorophenyl)-5,6-dihydro-9-methyl-4H-thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepin-2-yl]-2-propynyl]-6(5H)-phenanthridinone (9CI) (CA INDEX NAME)

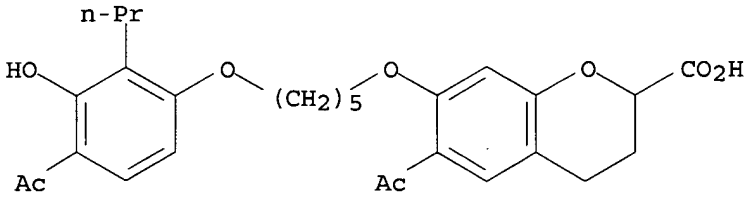
CM 1

CRN 140634-85-1
CMF C31 H22 Cl N5 O S



CM 2

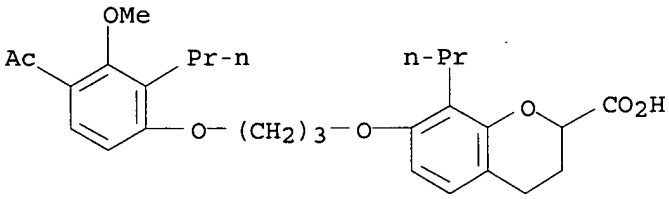
CRN 96566-25-5
CMF C28 H34 O8



AB A synergistic combination of platelet activating factor (PAF) antagonists with leukotriene D4 (LTD4) antagonists provides protection against allergic reactions, such as antigen-induced death. Guinea pigs were sensitized with an i.p. injection of ovalbumin in a saline soln. and administered with a combination of 5-[3-[4-(2-chlorophenyl)-9-methyl-6H-thieno[3,2-f]1,2,4]triazolo[4,3-a][1,4]diazepin-2-yl]-2-propynyl]phenanthridin-6(5H)-one (I) (PAF antagonist) and (E)-4-[3-[2-(4-cyclobutyl-2-thiazolyl)ethenyl]phenylamino]-2,2-diethyl-4-oxobutanoic acid (II) (LTD4 antagonist) at 1 mg/kg each before challenge with antigen; a survival rate from anaphylactic death at 120 min was 100

%, compared to 0 % for groups administered with I or II alone. Formulations contg. I and II combinations are given.

L3 ANSWER 71 OF 101 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:262600 CAPLUS
DOCUMENT NUMBER: 116:262600
TITLE: Drug matrix effect on the determination of residual solvents in bulk pharmaceuticals by wide-bore capillary gas chromatography
AUTHOR(S): Kersten, Brian S.
CORPORATE SOURCE: Searle Res. Dev., Skokie, IL, 60077, USA
SOURCE: Journal of Chromatographic Science (1992), 30(4), 115-19
CODEN: JCHSBZ; ISSN: 0021-9665
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **120072-59-5**
RL: ANST (Analytical study)
(residual solvents detn. in, by wide-bore capillary gas chromatog., drug matrix effect on)
RN 120072-59-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



AB A wide-bore capillary gas chromatog. method was developed to study the drug matrix effect on the detn. of residual solvents in bulk pharmaceuticals. A selective method is achieved on a Restek wide-bore (0.53-mm i.d. .times. 30 m) open-tubular fused-silica column coated with a 5-.mu.m film of 95% di-Me-5% di-Ph polysiloxane protected by a phenyl-Me siloxane deactivated, uncoated fused-silica guard column. Utilizing this method, several common process solvents in weakly acidic, weakly basic, and neutral drug matrixes are evaluated by recovery and linearity studies to show whether or not a drug matrix effect exists in their detn.

L3 ANSWER 72 OF 101 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:214350 CAPLUS
DOCUMENT NUMBER: 116:214350
TITLE: Preparation of 3,4-dihydro-7-[(carbamoylphenoxy)alkoxy]benzopyran-2-alkanoates and analogs as LTB4 antagonists
INVENTOR(S): Djuric, Stevan Wakefield; Docter, Stephen Hermann; Yu, Stella Siu Tzyy
PATENT ASSIGNEE(S): Searle, G. D., and Co., USA
SOURCE: PCT Int. Appl., 149 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9200011	A2	19920109	WO 1991-US4386	19910627
WO 9200011	A3	19920206		

W: AT, AU, BB, BG, BR, CA, CH, CS, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MC, MG, NL, NO, PL
RW: AT, BE, BF, BJ, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GN, GR, IT, LU, NL, SE, SN, TD, TG

US 5124350	A	19920623	US 1990-545430	19900628
AU 9185282	A1	19920123	AU 1991-85282	19910627
JP 05507720	T2	19931104	JP 1991-515594	19910627
JP 2942630	B2	19990830		
EP 593478	A1	19940427	EP 1991-916271	19910627
EP 593478	B1	19951206		

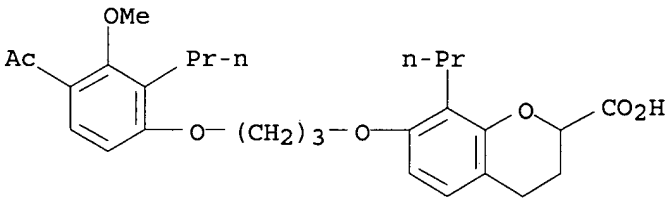
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE

AT 131165	E	19951215	AT 1991-916271	19910627
ES 2080334	T3	19960201	ES 1991-916271	19910627

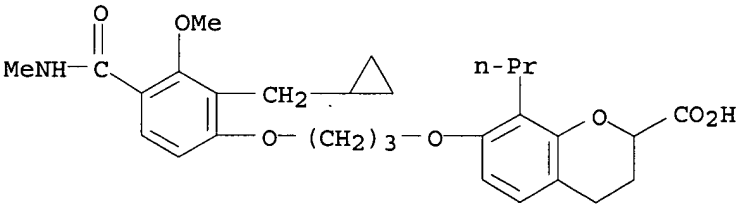
PRIORITY APPLN. INFO.: US 1990-545430 19900628
WO 1991-US4386 19910627

OTHER SOURCE(S): MARPAT 116:214350

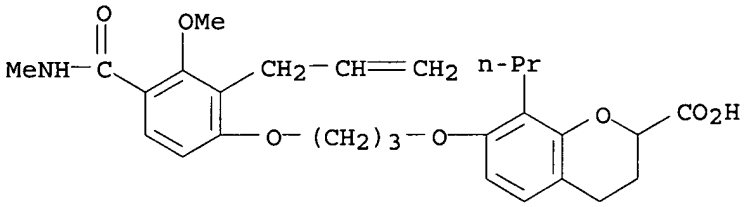
IT **120072-59-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 120072-59-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



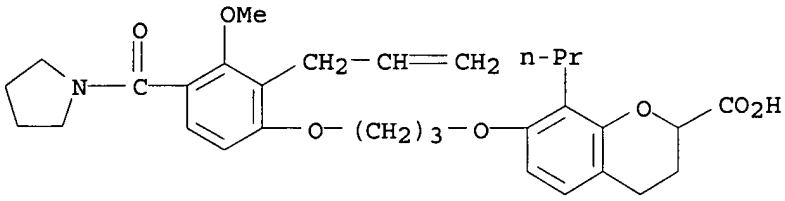
IT **141059-14-5P 141059-19-0P 141059-22-5P**
141059-25-8P 141059-28-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as LTB4 antagonist)
RN 141059-14-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[2-(cyclopropylmethyl)-3-methoxy-4-[(methylamino)carbonyl]phenoxy]propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



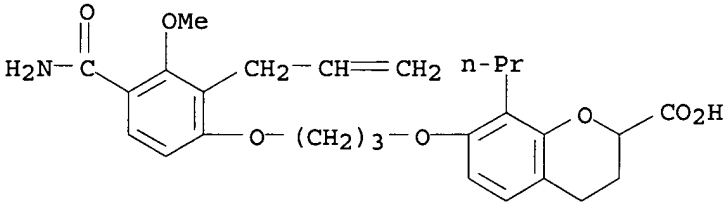
RN 141059-19-0 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 3,4-dihydro-7-[3-[3-methoxy-4-[(methylamino)carbonyl]-2-(2-propenyl)phenoxy]propoxy]-8-propyl- (9CI) (CA INDEX NAME)



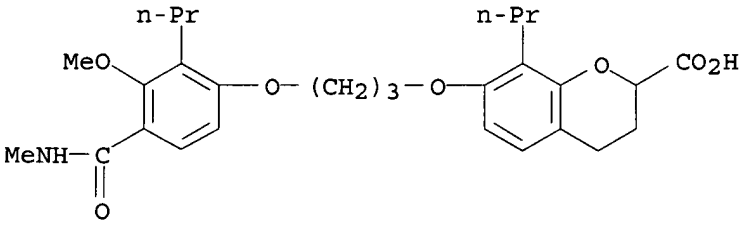
RN 141059-22-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 3,4-dihydro-7-[3-[3-methoxy-2-(2-propenyl)-4-(1-pyrrolidinylcarbonyl)phenoxy]propoxy]-8-propyl- (9CI) (CA INDEX NAME)



RN 141059-25-8 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[4-(aminocarbonyl)-3-methoxy-2-(2-propenyl)phenoxy]propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



RN 141059-28-1 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 3,4-dihydro-7-[3-[3-methoxy-4-[(methylamino)carbonyl]-2-propylphenoxy]propoxy]-8-propyl- (9CI) (CA INDEX NAME)



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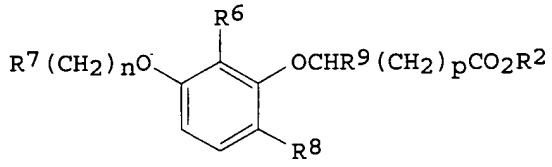
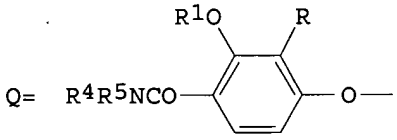
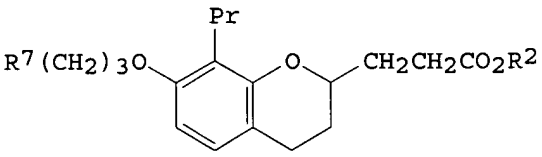


I

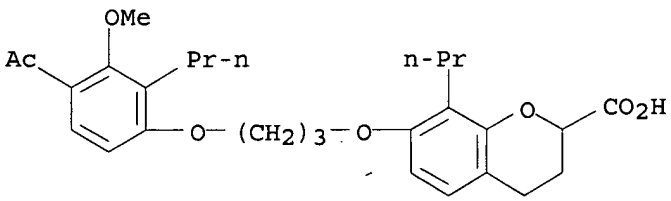




II

AB Title compds. {I; R2 = H, alkyl; R6 = alkyl; R7 = carbamoylphenoxy group Q; R = alkyl, alkenyl, alkynyl, (CH2)mR3; R1 = alkyl; R3 = cycloalkyl; R4,R5 = H, alkyl; NR4R5 = heterocyclyl; R8, R9 = H; R8R9 = CH2CH2; m = 1,2; n = 3-7; p = 0-6] were prepd. Thus, benzopyranpropanoate II (R2 = Me, R7 = iodo) (prepn. given) was condensed with QH (R = allyl, R1 = R5 = H, R4 = Me) (prepn. given) to give II (R7 = Q, R = alkyl, R4 = Me, R5 = H) (III; R2 = Me, R1 = H) which was converted in 2 steps to III (R2 = H, R1 = Me). The latter was 8.9 times as effective as 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl-2H-1-benzopyran-2-carboxylic acid in inhibition of binding of LTB4 at human neutrophils in vitro.

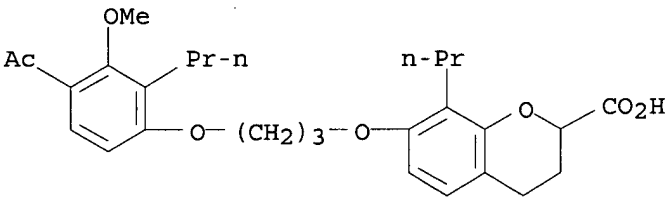
L3 ANSWER 73 OF 101 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:145642 CAPLUS
DOCUMENT NUMBER: 116:145642
TITLE: Induction of colitis in rats by 2,2'-azobis[2-amidinopropane] dihydrochloride
AUTHOR(S): Tamai, Hiroshi; Levin, Stuart; Gaginella, Timothy S.
CORPORATE SOURCE: Searle Res. and Dev., Skokie, IL, 60077, USA
SOURCE: Inflammation (New York, NY, United States) (1992), 16(1), 69-81
CODEN: INFLD4; ISSN: 0360-3997
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **120072-59-5**, SC-41930
RL: BIOL (Biological study)
(azobis(amidinopropane)-induced colitis prevention by)
RN 120072-59-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



AB 2,2'-Azobis[2-amidinopropane] dihydrochloride (AAPH), an azo compd. that generates free radicals in vitro, was administered intrarectally to rats.

Acute mucosal injury was assessed histol. by light microscopy and biochem. by myeloperoxidase (MPO) activity. Intrarectal administration of AAPH (60, 90, and 150 mg/kg) caused erythema, edema, and histol. verifiable mucosal inflammation. MPO activity was increased 9-18-fold above the control level. The levels of thiobarbituric acid reactants and sulfhydryls were significantly increased and decreased, resp., by 90 mg/kg AAPH. Sulfasalazine, 5-aminosalicylic acid, the LTB4 receptor antagonist SC 41930, and the antioxidant glutathione prevented the inflammation. This model of mucosal inflammation may be useful in evaluating new therapeutic agents for the treatment of inflammatory bowel disease.

L3 ANSWER 74 OF 101 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:120578 CAPLUS
DOCUMENT NUMBER: 116:120578
TITLE: Multiple actions of the leukotriene B4 receptor antagonist SC-41930
AUTHOR(S): Villani-Price, D.; Yang, D. C.; Walsh, R. E.; Fretland, D. J.; Keith, R. H.; Kocan, G.; Kachur, J. F.; Gaginella, T. S.; Tsai, B. S.
CORPORATE SOURCE: Searle Res. and Dev., Skokie, IL, 60077, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (1992), 260(1), 187-91
CODEN: JPETAB; ISSN: 0022-3565
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **120072-59-5**, SC 41930
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inflammation inhibition by, mechanism of)
RN 120072-59-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



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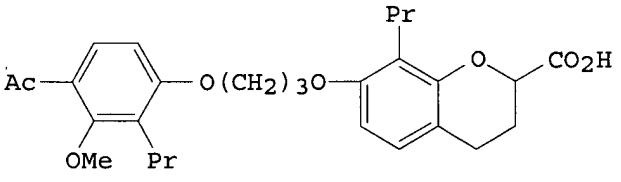


I

AB SC-41930 (I), a leukotriene B4 (LTB4) receptor antagonist with anti-inflammatory activity in animal models of colitis, was evaluated for effects on superoxide, LTB4 and prostaglandin E2 prodn. SC-41930 inhibited human neutrophil (PMN) superoxide generation maximally stimulated by f-Met-Leu-Phe (IC50 4 .mu.M) and C5a (IC50 .apprx.12 .mu.M). Moreover, postreceptor stimulation of superoxide prodn. by NaF (a G protein activator), but not by phorbol myristate acetate, was significantly inhibited by SC-41930, indicating that SC-41930 may act via

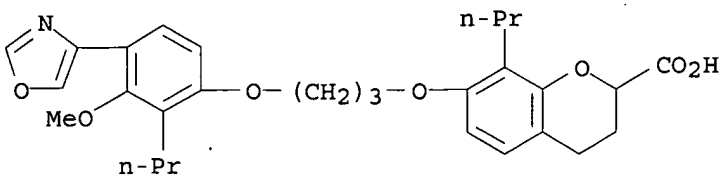
attenuation of a G protein-mediated signal transduction. SC-41930 also inhibited A23187-stimulated LTB4 prodn. (IC50 5.3 .mu.M) in human PMN as well as LTB4 (IC50 2.1 .mu.M) and prostaglandin E2 (IC50 2.9 .mu.M) prodn. in HL-60 cells. When coinjected intradermally (400 .mu.g/site), SC-41930 inhibited A23187-stimulated increases in LTB4 levels in guinea pig skin. SC-41930 inhibited human synovial phospholipase A2 (IC50 72 .mu.M), A23187-stimulated 5-hydroxyeicosatetraenoic acid prodn. in human PMN (IC50 8.5 .mu.M), and rat peritoneal leukotriene A4 hydrolase (IC50 20 .mu.M), but not ram seminal vesicle cyclooxygenase. The results suggest that the anti-inflammatory activity of SC-41930 could be attributed to postreceptor inhibition of inflammatory mediator prodn. by PMN and other cells in addn. to antagonism of PMN LTB4 receptors.

L3 ANSWER 75 OF 101 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:83676 CAPLUS
DOCUMENT NUMBER: 116:83676
TITLE: Preparation of heterocycles containing alkoxy-substituted dihydrobenzopyran-2-carboxylic acids as leukotriene B4 (LTB4) antagonists
INVENTOR(S): Djuric, Stevan Wakefield; Penning, Thomas Dale; Snyder, James Patrick
PATENT ASSIGNEE(S): Searle, G. D., and Co., USA
SOURCE: PCT Int. Appl., 90 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

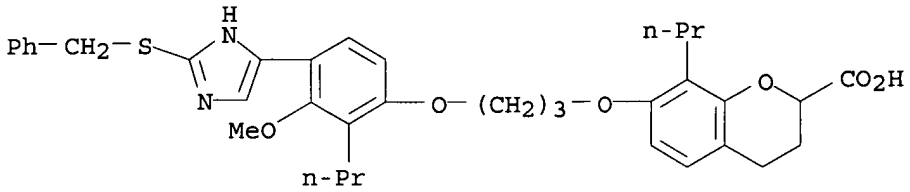
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9117160	A1	19911114	WO 1991-US2981	19910501
W: AT, AU, BB, BG, BR, CA, CH, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MC, MG, MW, NL, NO, PL, RO, SD, SE, SU, US				
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IT, LU, ML, MR, NL, SE, SN, TD, TG				
US 5073562	A	19911217	US 1990-521777	19900510
CA 2082500	AA	19911111	CA 1991-2082500	19910501
AU 9179020	A1	19911127	AU 1991-79020	19910501
AU 647487	B2	19940324		
EP 527922	A1	19930224	EP 1991-910026	19910501
EP 527922	B1	19950308		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 05507084	T2	19931014	JP 1991-509388	19910501
ES 2069295	T3	19950501	ES 1991-910026	19910501
IL 98090	A1	19950731	IL 1991-98090	19910509
ZA 9103546	A	19920729	ZA 1991-3546	19910510
US 5192782	A	19930309	US 1991-759272	19910913
US 5212198	A	19930518	US 1992-958632	19921009

PRIORITY APPLN. INFO.: US 1990-521777 19900510
WO 1991-US2981 19910501
US 1991-759272 19910913

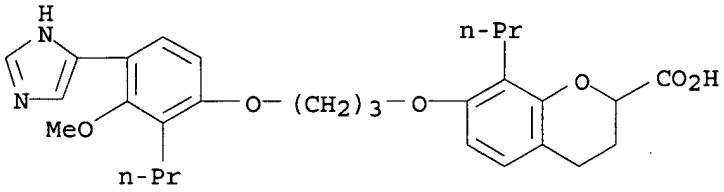
OTHER SOURCE(S): MARPAT 116:83676
IT **138828-24-7P 138828-27-0P 138828-28-1P**
138828-29-2P 138828-31-6P 138828-33-8P
138828-36-1P 138828-39-4P 138828-42-9P
138828-44-1P 138828-46-3P 138828-47-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as LTB4 antagonist)
RN 138828-24-7 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 3,4-dihydro-7-[3-[3-methoxy-4-(4-oxazolyl)-2-propylphenoxy]propoxy]-8-propyl- (9CI) (CA INDEX NAME)



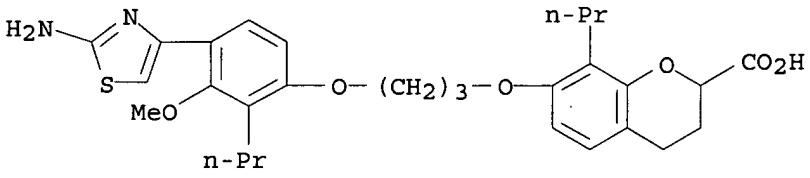
RN 138828-27-0 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 3,4-dihydro-7-[3-[3-methoxy-4-[2-[(phenylmethyl)thio]-1H-imidazol-4-yl]-2-propylphenoxy]propoxy]-8-propyl- (9CI) (CA INDEX NAME)



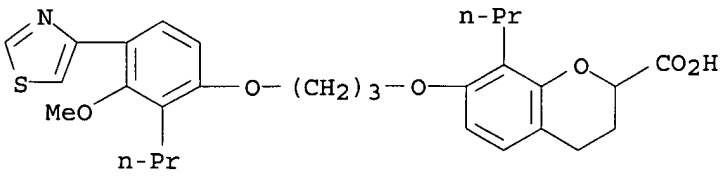
RN 138828-28-1 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 3,4-dihydro-7-[3-[4-(1H-imidazol-4-yl)-3-methoxy-2-propylphenoxy]propoxy]-8-propyl- (9CI) (CA INDEX NAME)



RN 138828-29-2 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[4-(2-amino-4-thiazolyl)-3-methoxy-2-propylphenoxy]propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)

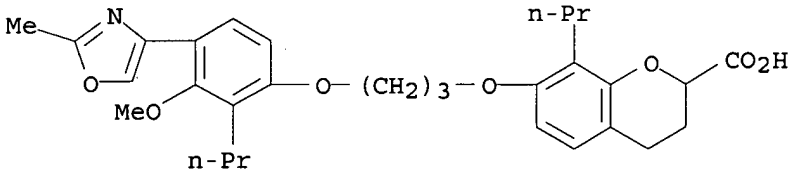


RN 138828-31-6 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 3,4-dihydro-7-[3-[3-methoxy-2-propyl-4-(4-thiazolyl)phenoxy]propoxy]-8-propyl- (9CI) (CA INDEX NAME)

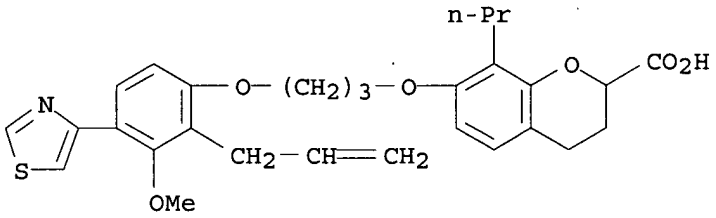


RN 138828-33-8 CAPLUS

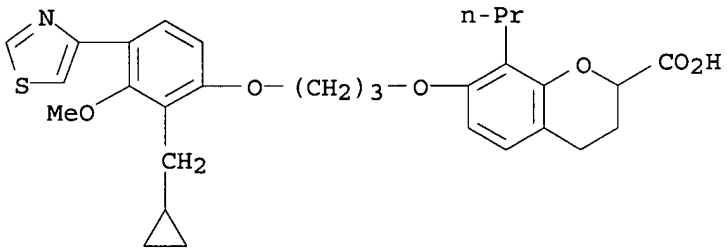
CN 2H-1-Benzopyran-2-carboxylic acid, 3,4-dihydro-7-[3-[3-methoxy-4-(2-methyl-4-oxazolyl)-2-propylphenoxy]propoxy]-8-propyl- (9CI) (CA INDEX NAME)



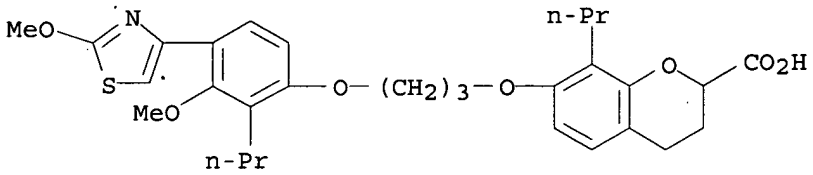
RN 138828-36-1 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 3,4-dihydro-7-[3-[3-methoxy-2-(2-propenyl)-4-(4-thiazolyl)phenoxy]propoxy]-8-propyl- (9CI) (CA INDEX NAME)



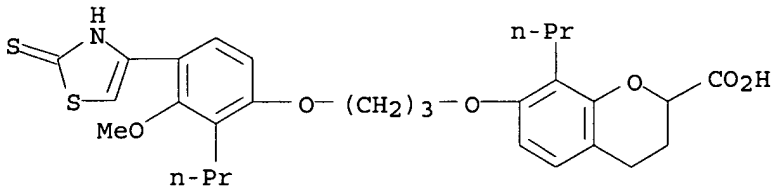
RN 138828-39-4 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[2-(cyclopropylmethyl)-3-methoxy-4-(4-thiazolyl)phenoxy]propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



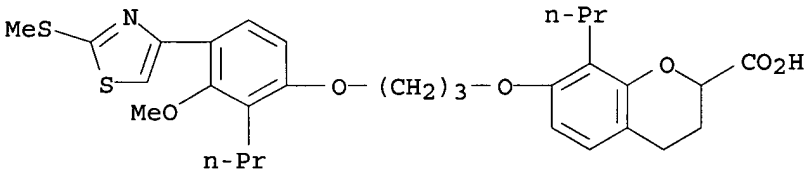
RN 138828-42-9 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 3,4-dihydro-7-[3-[3-methoxy-4-(2-methoxy-4-thiazolyl)-2-propylphenoxy]propoxy]-8-propyl- (9CI) (CA INDEX NAME)



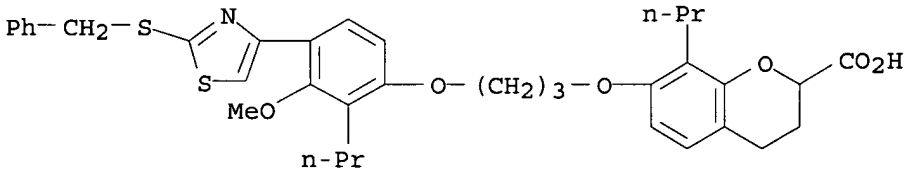
RN 138828-44-1 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[4-(2,3-dihydro-2-thioxo-4-thiazolyl)-3-methoxy-2-propylphenoxy]propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



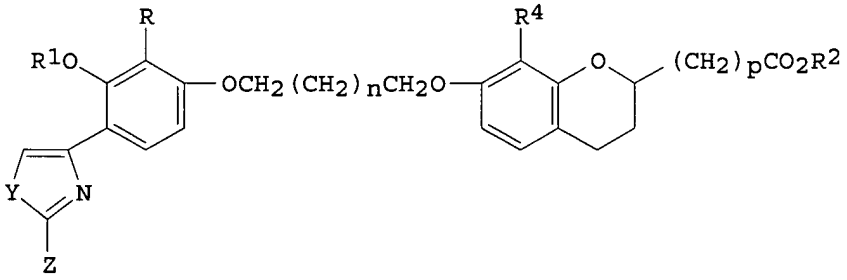
RN 138828-46-3 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 3,4-dihydro-7-[3-[3-methoxy-4-[2-(methylthio)-4-thiazolyl]-2-propylphenoxy]propoxy]-8-propyl- (9CI) (CA INDEX NAME)



RN 138828-47-4 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 3,4-dihydro-7-[3-[3-methoxy-4-[2-[(phenylmethyl)thio]-4-thiazolyl]-2-propylphenoxy]propoxy]-8-propyl- (9CI) (CA INDEX NAME)



GI



I

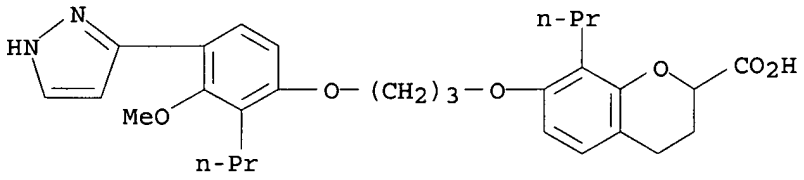
AB Title compds. I (R = C2-6 alkyl, C2-6 alkenyl, C2-6 alkynyl, R3(CH2)m, wherein R3 = C3-5 cycloalkyl, m = 1,2; R1 = C1-4 alkyl; R2 = H, C1-5 alkyl; R4 = C1-6 alkyl; n = 1-5; p = 0-6; Y = NH, O, S; Z = H, C1-4 alkyl, C1-4 alkoxy, R5R4N wherein R4, R5 = H, C1-4 alkyl, R6S wherein R6 = H, PhCH2, C1-4 alkyl), stereoisomers and salts thereof, are prepd. I as LTB4 antagonists are useful as antiinflammatory agents and in treatment of LTB4-mediated conditions. The 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl-2H-1-benzopyran-2-carboxylate (prepn. given) was converted to the 2-hydroxy-1-oxoethyl deriv. which was treated with (F3CSO2)2O to give the 2-(trifluoromethylsulfonyloxy deriv. This compd. was stirred with HCONH2 and DMF to give I (R = R4 = Pr, R1 =

R2 = Me, Y = O, Z = H, n = 1, p = 0) which was stirred with LiOH to give I (R = R4 = Pr, R1 = Me, R2 = Z = H, Y = O, n = 1, p = 0) (II). II and other title compds. showed LTB4 antagonism.

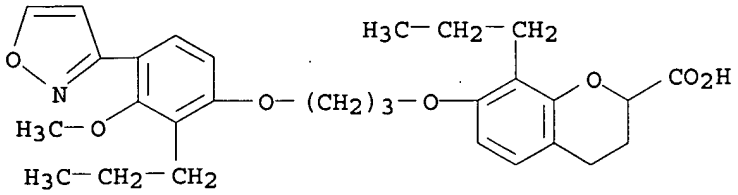
L3 ANSWER 76 OF 101 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:6555 CAPLUS
DOCUMENT NUMBER: 116:6555
TITLE: Preparation of [(azolylphenoxy)alkoxy]benzopyrancarboxylates as antiinflammatories
INVENTOR(S): Djuric, Stevan W.; Penning, Thomas D.
PATENT ASSIGNEE(S): Searle, G. D., and Co., USA
SOURCE: U.S., 11 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5051438	A	19910924	US 1990-524765	19900516
CA 2083040	AA	19911117	CA 1991-2083040	19910503
WO 9117989	A1	19911128	WO 1991-US3068	19910503
W: AT, AU, BB, BG, BR, CA, CH, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MC, MG, MW, NL, NO, PL, RO, SD, SE, SU, US				
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IT, LU, ML, MR, NL, SE, SN, TD, TG				
AU 9178925	A1	19911210	AU 1991-78925	19910503
EP 528935	A1	19930303	EP 1991-909729	19910503
EP 528935	B1	19941019		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 05506440	T2	19930922	JP 1991-509234	19910503
ES 2062792	T3	19941216	ES 1991-909729	19910503

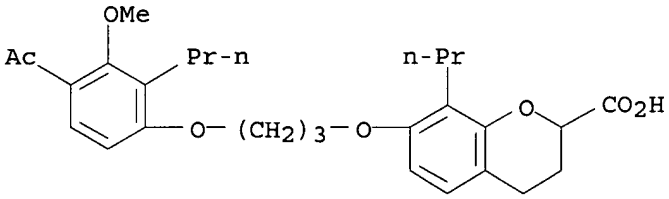
PRIORITY APPLN. INFO.: US 1990-524765 19900516
WO 1991-US3068 19910503
OTHER SOURCE(S): MARPAT 116:6555
IT **137837-12-8P 137856-08-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as antiinflammatory)
RN 137837-12-8 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 3,4-dihydro-7-[3-[3-methoxy-2-propyl-4-(1H-pyrazol-3-yl)phenoxy]propoxy]-8-propyl- (9CI) (CA INDEX NAME)



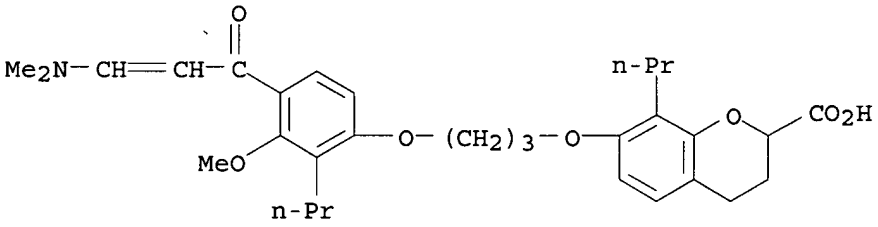
RN 137856-08-7 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 3,4-dihydro-7-[3-[4-(3-isoxazolyl)-3-methoxy-2-propylphenoxy]propoxy]-8-propyl- (9CI) (CA INDEX NAME)



IT **120072-59-5P 137837-15-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as intermediate for antiinflammatory)
RN 120072-59-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



RN 137837-15-1 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[4-[3-(dimethylamino)-1-oxo-2-propenyl]-3-methoxy-2-propylphenoxy]propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



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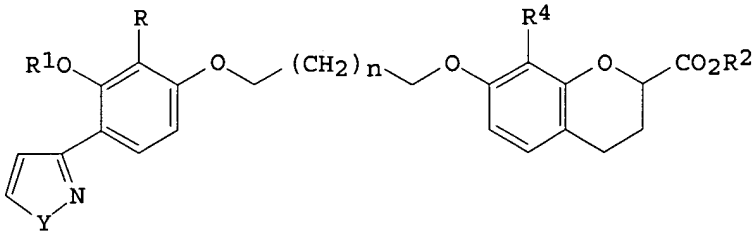
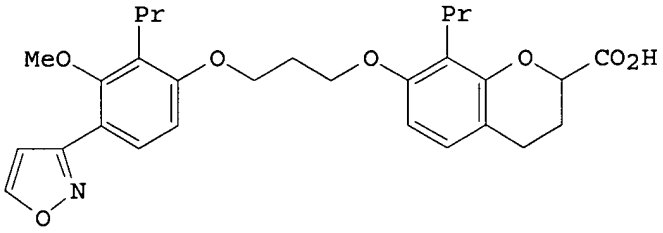


I



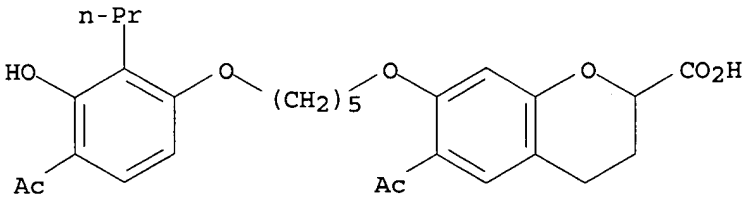
II

AB Title compds. (I; R = alkyl, alkenyl, alkynyl, cycloalkylalkyl; R1, R4 = alkyl; R2 = H, alkyl; Y = NH, O; n = 1-5), were prepd. Thus, Me 7-[3-(4-acetyl-3-hydroxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl-2H-1-benzopyran-2-carboxylate was O-methylated with MeI/K2CO3 in acetone. The product was condensed with Me2NCH(OMe)2 in DMF and the enaminone product was refluxed with H2NOH.HCl in MeOH/H2O to give, after sapon., title compd. II. II antagonized LTB4-induced chemotaxis of human neutrophils with 0.25 of the potency of 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl-2H-1-benzopyran-2-carboxylic acid.

L3 ANSWER 77 OF 101 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:721 CAPLUS
DOCUMENT NUMBER: 116:721
TITLE: Pheroxypentyloxy-3,4-dihydro-2H-1-benzopyran derivatives for treatment of leukotriene-induced inflammation of the intestinal mucosa
PATENT ASSIGNEE(S): Hoffmann-La Roche, F. A.-G., Switz.
SOURCE: Austrian, 20 pp.
CODEN: AUXXAK
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

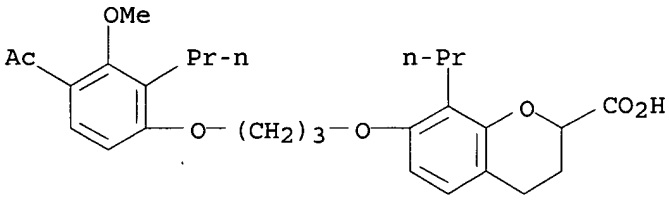
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
AT 392902	B	19910710	AT 1987-2643	19871008
AT 8702643	A	19901215		

OTHER SOURCE(S): MARPAT 116:721
IT **96566-25-5 131147-29-0 131147-29-0D**, esters
RL: BIOL (Biological study)
(leukotriene-induced intestinal mucosa inflammation treatment with)
RN 96566-25-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 6-acetyl-7-[[5-(4-acetyl-3-hydroxy-2-propylphenoxy)pentyl]oxy]-3,4-dihydro- (9CI) (CA INDEX NAME)



RN 131147-29-0 CAPLUS
RN 131147-29-0 CAPLUS
AB The title compds., esp. racemic 6-acetyl-7-[5-(4-acetyl-3-hydroxy-2-propylphenyloxy)pentyloxy]-3,4-dihydro-2H-1-benzopyran-2-carbonic acid (I), are prepd. as oral, rectal, or parenteral formulations. I at 10-100 mg/kg orally was effective against clindamycin-induced colitis in hamsters.

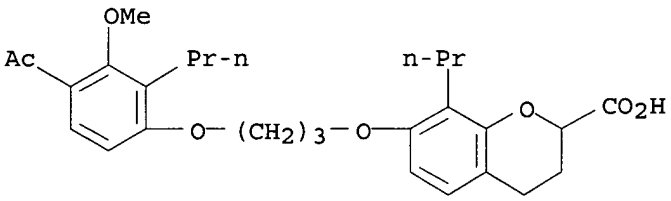
L3 ANSWER 78 OF 101 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:654087 CAPLUS
DOCUMENT NUMBER: 115:254087
TITLE: Effects of two leukotriene B4 (LTB4) receptor antagonists (LY255283 and SC-41930) on LTB4-induced human neutrophil adhesion and superoxide production
AUTHOR(S): Schultz, R. M.; Marder, P.; Spaethe, S. M.; Herron, D. K.; Sofia, M. J.
CORPORATE SOURCE: Lilly Res. Lab., Indianapolis, IN, 46285, USA
SOURCE: Prostaglandins, Leukotrienes and Essential Fatty Acids (1991), 43(4), 267-71
CODEN: PLEAEU; ISSN: 0952-3278
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **120072-59-5**, SC 41930
RL: BIOL (Biological study)
(superoxide formation and adhesion by neutrophils response to)
RN 120072-59-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



AB LTB4 induces a no. of functional changes in human neutrophils, including both superoxide release and CD11b/CD18 (Mo1)-mediated adherence to various substrates, such as keyhole limpet hemocyanin (KLH). These effects are both time- and concn.-dependent. Neutrophil adhesion was at least 10-fold more sensitive to the stimulatory action of LTB4 than superoxide prodn. Two LTB4 receptor antagonists, LY255283 and the sodium salt of SC-41930 were evaluated for effects on human neutrophil superoxide prodn. and adhesion. Despite being more sensitive to LTB4-induced stimulation, neutrophil adhesion was at least 100-fold less sensitive to inhibition by LY255283 and SC-41930 than superoxide prodn. Both LTB4 receptor antagonists behaved similarly in these models. These compds. did not inhibit neutrophil responses induced by granulocyte/macrophage colony-stimulating factor (GM-CSF).

L3 ANSWER 79 OF 101 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:597978 CAPLUS

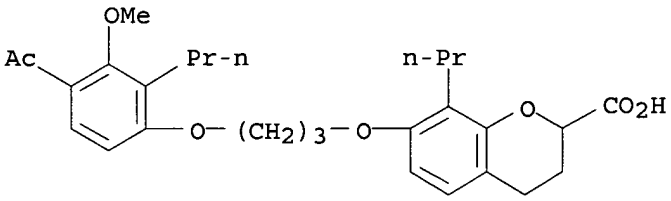
DOCUMENT NUMBER: 115:197978
TITLE: The antiinflammatory agent SC-41930 inhibits granulocyte infiltration of the rodent dermis induced by 6-trans-leukotriene B4
AUTHOR(S): Fretland, D. J.; Widomski, D. L.; Anglin, C. P.; Gaginella, T. S.
CORPORATE SOURCE: Searle Res. Dev., Skokie, IL, 60077, USA
SOURCE: Prostaglandins, Leukotrienes and Essential Fatty Acids (1991), 44(1), 61-5
CODEN: PLEAEU; ISSN: 0952-3278
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **120072-59-5**, SC-41930
RL: BIOL (Biological study)
(granulocyte infiltration stimulation by leukotriene B4 inhibition by, inflammation inhibition in relation to)
RN 120072-59-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



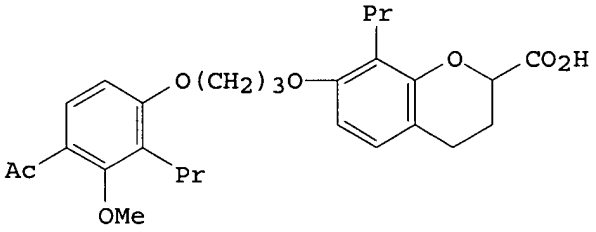
AB Granulocyte diapedesis in response to the generation of defined chemotaxins such as leukotriene B4 (LTB4), 12(R)-hydroxyeicosatetraenoic acid [12(R)-HETE], C5a, platelet activating factor and others is a hallmark of the inflammatory process that is thought to contribute to the tissue pathol. seen in a no. of diseases. 6-trans-LTB4 arises through the myeloperoxidase (MPO)-HETE. The intradermal (i.d.) injection of 6-trans-LTB4 induces a dose and time dependent influx of granulocytes into the guinea-pig (Hartley) dermis. When various doses of the LTB4 receptor antagonist and antiinflammatory agent, SC-41930 {7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)-propoxy]-3,4-dihydro-8-propyl-2H-1-benzopyran-2-carboxylic acid} given 30 min ahead of i.d. injection of 6-trans-LTB4 (10 .mu.g/i.d. site), granulocyte infiltration, as assessed by dermal levels of the neutrophil marker enzyme MPO was inhibited with an ED50 value of 9.8 mg/kg in the guinea-pig. When various doses (10-25 .mu.g) 6-trans-LTB4 were injected in the mouse (CD-1) dermis, there was a dose-related increase in granulocyte accumulation at 4 h. Furthermore when mice were pretreated (-30 min) with SC-41930 (1 mg/kg) orally, the trafficking of granulocytes was inhibited ($p < .01$) as assessed by dermal MPO levels. SC-41930 orally inhibits 6-trans-LTB4-induced granulocyte accumulation in the guinea-pig more potently than against the response to 12(R)-HETE(ED50:13.4 mg/kg) but less potently than against LTB4 (ED50:0.6 mg/kg). These multiple activities may contribute to this compd.'s potential as an inflammation inhibitor.

L3 ANSWER 80 OF 101 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:549984 CAPLUS
DOCUMENT NUMBER: 115:149984
TITLE: Effect of the leukotriene B4 receptor antagonist, SC-41930, on experimental allergic encephalomyelitis (EAE) in the guinea pig
AUTHOR(S): Fretland, D. J.; Widomski, D. L.; Shone, R. L.; Levin, S.; Gaginella, T. S.
CORPORATE SOURCE: Dep. Pathol., Searle Res. and Dev., Skokie, IL, 60077, USA

SOURCE: Agents and Actions (1991), 34(1-2), 172-4
CODEN: AGACBH; ISSN: 0065-4299
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **120072-59-5**, SC-41930
RL: BIOL (Biological study)
(multiple sclerosis treatment with, allergic encephalomyelitis model in relation to)
RN 120072-59-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



GI



I

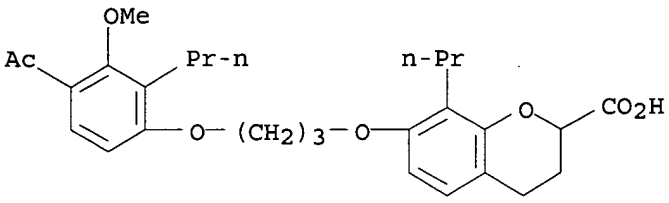
AB The accepted model for the human demyelinating disease, multiple sclerosis (MS), is exptl. allergic encephalomyelitis (EAE). The ability of SC-41930 (I) to modulate the symptoms of acute EAE was examd. in guinea pigs. Animals were pretreated with SC-41930 (20 mg/kg, i.p.) for two days followed by thrice-weekly maintenance. At day 52, a significant no. of the SC-41930-treated animals were alive as compared to EAE alone. Control animals had an increase in body wt. while EAE animals lost over 20% ($p<0.5$) of their body wt. by day 18. SC-41930-treatment significantly reduced, but did not completely inhibit the cachectic response. The results indirectly implicate LTB4 in the pathogenesis of EAE. Agents that modify this model may be useful in the treatment of human MS.

L3 ANSWER 81 OF 101 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:549983 CAPLUS
DOCUMENT NUMBER: 115:149983
TITLE: Modulation of the chemotactic properties of complement fragments C5a and C3 by the anti-inflammatory agent, SC-41930
AUTHOR(S): Fretland, D. J.; Widomski, D. L.; Anglin, C. P.; Levin, S.; Gaginella, T. S.
CORPORATE SOURCE: Dep. Pathol., Searle Res. and Dev., Skokie, IL, 60077, USA
SOURCE: Agents and Actions (1991), 34(1-2), 5-7
CODEN: AGACBH; ISSN: 0065-4299
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **120072-59-5**, SC-41930
RL: BIOL (Biological study)

(complement fragment-induced chemotaxis response to, inflammation inhibition in relation to)

RN 120072-59-5 CAPLUS

CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



AB Cleavage of the fifth component of complement yields C5a, a potent neutrophil (PMN) and eosinophil chemoattractant, and modulator of microvascular permeability. Similarly, but to a lesser degree, C3 increases vascular permeability and histamine release. SC-41930 (7-[3-(4-actyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl-2H-1-benzopyran-2-carboxylic acid), an orally-active antiinflammatory agent was tested in an in vivo model of dermal PMN chemotaxis induced by r-hu-C45a and hu-C3. Intradermal injection of C5a in the guinea pig resulted in a significant dose-dependent influx of PMNs at 4 h as assessed by the dermal levels of myeloperoxidase (MPO). SC-41930(20 mg/kg) given orally to guinea pigs with intradermal injections of 1 .mu.g C5a significantly reduced dermal MPO content SC-41930 was less potent against C3, requiring 40 mg/kg to significantly reduce dermal MPO levels. Agents such as SC-41930, which nullify complement's proinflammatory properties, may well have therapeutic potential.

L3 ANSWER 82 OF 101 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1991:221333 CAPLUS

DOCUMENT NUMBER: 114:221333

TITLE: Inflammation of guinea pig dermis. Effects of leukotriene B4 receptor antagonist, SC-41930

AUTHOR(S): Fretland, D. J.; Widomski, D. L.; Zemaitis, J. M.; Walsh, R. E.; Levin, S.; Djuric, S. W.; Shone, R. L.; Tsai, B. S.; Gaginella, T. S.

CORPORATE SOURCE: Dep. Gastrointest. Dis., Searle Res. and Dev., Skokie, IL, USA

SOURCE: Inflammation (New York, NY, United States) (1990), 14(6), 727-39
CODEN: INFLD4; ISSN: 0360-3997

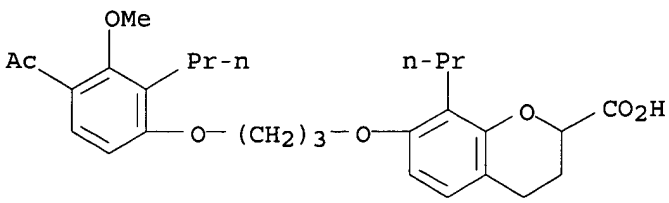
DOCUMENT TYPE: Journal

LANGUAGE: English

IT **120072-59-5**, SC 41930
RL: BIOL (Biological study)
(skin inflammation response to topical, psoriasis treatment in relation to)

RN 120072-59-5 CAPLUS

CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



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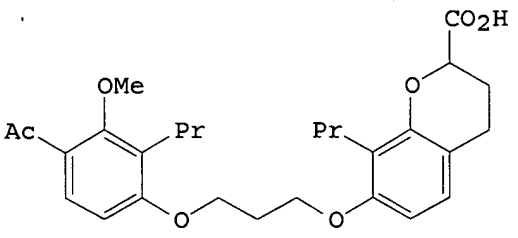
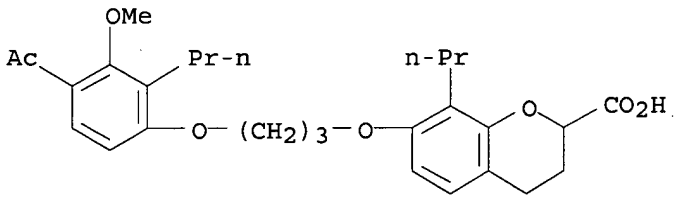


I

AB Neutrophil (PMNL) infiltration is a prominent feature of human psoriasis. Psoriatic skin lesions contain abnormally high amts. of leukotriene B4 (LTB4), itself a potent PMNL chemoattractant both in vivo and in vitro. SC-41930 (I), an orally active LTB4 receptor antagonist, was tested topically in models of skin inflammation induced by 200 nmol of the calcium ionophore A23187 or 200 .mu.g phorbol-12-myristate-13-acetate (PMA) applied topically to the guinea pig ear as assessed by ear wt., levels of the PMNL marker enzyme myeloperoxidase (MPO), and histol. examn. (PMA model) at 4 and 18 h resp. When coapplied topically with A23187 or PMA, I inhibited epidermal inflammation with ED50 values of 0.6 and 4 mg, resp. I treatment also was assocd. with lowered dermal LTB4 levels in both models. The PMA-induced skin inflammation model also was assessed histolog. and revealed acanthosis, edema, PMNL infiltration, and rete ridge prominence as long as 96 h after a single application that was completely inhibited by I topical coapplication. Furthermore, oral treatment (40 mg/kg) reduced edema and inflammatory cell infiltration in both models. These models possess many of the characteristics of human psoriass, and agents such as I that demonstrate activity in those models may well have therapeutic utility in the treatment of human psoriasis.

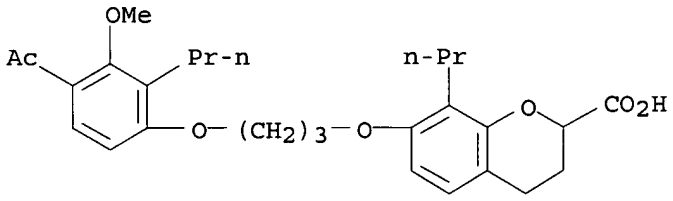
L3 ANSWER 83 OF 101 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:178176 CAPLUS
DOCUMENT NUMBER: 114:178176
TITLE: A23187-induced pulmonary gas trapping and inflammation in the guinea pig
AUTHOR(S): Stengel, Peter W.; Williams, G. D.; Silbaugh, S. A.
CORPORATE SOURCE: Lilly Res. Lab., Indianapolis, IN, 46285, USA
SOURCE: Agents and Actions (1991), 32(3-4), 270-6
CODEN: AGACBH; ISSN: 0065-4299
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **120072-59-5**, SC 41930
RL: BIOL (Biological study)
(lung obstruction and inflammation from A 23187 response to)
RN 120072-59-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



AB A brief A23187 aerosol exposure produced prolonged airway obstruction with granulocyte accumulation in conscious guinea pigs. Aminophylline,

atropine, pyrilamine, salbutamol, SC-41930 (a leukotriene B4 antagonist) and WEB 2086 (a platelet-activating factor antagonist) were administered i.v. to evaluate their ability to prevent these changes. Inhaled salbutamol was also assessed. Aminophylline, atropine, and salbutamol (i.v. and aerosol) inhibited the A23187-induced pulmonary gas trapping. Pyrilamine, SC-41930 and WEB 2086 did not influence this airway-obstructive effect. Only atropine, inhaled salbutamol and SC-41930 inhibited the cell influx, while pyrilamine potentiated the inflammation. Apparently, A23187 produces a sustained bronchospasm and an intense granulocyte accumulation. The treatment agents tested differ considerably in their ability to alter A23187-induced obstruction and inflammation.

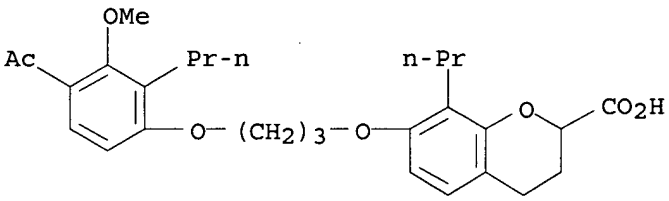
L3 ANSWER 84 OF 101 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:157171 CAPLUS
DOCUMENT NUMBER: 114:157171
TITLE: SC-41930, a leukotriene B4 receptor antagonist, inhibits 12(S)-hydroxyeicosatetraenoic acid (12(S)-HETE) binding to epidermal cells
AUTHOR(S): Kemeny, I.; Ruzicka, T.
CORPORATE SOURCE: Dep. Dermatol., Univ. Munich, Munich, 8000/2, Germany
SOURCE: Agents and Actions (1991), 32(3-4), 339-42
CODEN: AGACBH; ISSN: 0065-4299
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **120072-59-5**, SC-41930
RL: BIOL (Biological study)
(hydroxyeicosatetraenoic acid receptors antagonism by, in epidermal cells of humans)
RN 120072-59-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



AB SC-41930, 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)-propoxyl]-3,4-dihydro-8-propyl-2H-1-benzopyran-2-carboxylic acid, a potent leukotriene-B4 (LTB4) receptor antagonist, inhibits in vivo 12-hydroxyeicosatetraenoic acid (12-HETE)-induced neutrophil infiltration, suggesting a potential 12-HETE receptor antagonist effect, as well. Since 12-HETE is assumed to have a pathophysiol. role in inflammatory skin diseases, and epidermal cells possess high affinity binding sites for 12(S)-HETE, the effect of SC-41930 on 12(S)-HETE binding to the human epidermal cell line, SCL-II was studied. SC-41930 antagonized the 12(S)-HETE binding to SCL-II cells with a Ki of 480 nM. This Ki value is similar to that obtained for the inhibition of LTB4 binding to human neutrophils. Those results show that SC-41930, in addn. to its LTB4 receptor antagonist effect, exhibits 12-HETE receptor antagonist effect as well, and therefore may be of benefit in skin diseases with elevated 12-HETE levels.

L3 ANSWER 85 OF 101 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:35615 CAPLUS
DOCUMENT NUMBER: 114:35615
TITLE: Effect of the leukotriene B4 receptor antagonist SC-41930 on colonic inflammation in rat, guinea pig and rabbit
AUTHOR(S): Fretland, Donald J.; Widomski, Deborah; Tsai, Bie

Shung; Zemaitis, Jeanne M.; Levin, Stuart; Djuric, Stevan W.; Shone, Robert L.; Gaginella, Timothy S.
CORPORATE SOURCE: Dep. Gastrointest. Dis. Res., Searle Res. and Dev., Skokie, IL, 60077, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (1990), 255(2), 572-6
CODEN: JPETAB; ISSN: 0022-3565
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **120072-59-5**, SC 41930
RL: BIOL (Biological study)
(colon inflammation prevention by, as leukotriene B4 antagonist, in inflammatory bowel disease model)
RN 120072-59-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



AB Inflammatory bowel disease is a chronic inflammatory disorder of the gastrointestinal tract that includes ulcerative colitis and Crohn's disease. Leukotriene B4 is thought to be a prominent proinflammatory mediator in these diseases, in that leukotriene B4 levels are increased in the colonic mucosa of inflammatory bowel disease patients and there is increased polymorphonuclear leukocyte infiltration of these tissues. The efficacy of 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)-3,4-dihydro-8-propyl-2H-1-benzopyran-2-carboxylic acid (SC-41930), a potent, orally active leukotriene B4 receptor antagonist, in a model of inflammatory bowel disease was examd. Colonic mucosal inflammation was induced in rats, guinea pig and rabbits by rectal instillation of a dil. soln. of acetic acid. Twenty-four hours later, mucosal levels of myeloperoxidase (a marker enzyme for neutrophil infiltration) and extravasation of i.v. administered Evans blue dye (a marker of vascular disruption and increased permeability) were measured. Tissues were also evaluated histol. The animals received either SC-41930 or vehicle, intrarectally, 30 min after or 1 h before and 1 h after the acetic acid. When given 30 min after acetic acid instillation SC-41930 prevented the rise in myeloperoxidase and dye extravasation obsd. in the acetic acid inflamed tissue. The SC-41930-treated tissues were less edematous and had fewer neutrophils within the subepithelial space. Median ED (ED50) values for vascular protection were approx. 20 mg/kg for both rat and guinea pig. ED50 values for inhibition of granulocyte accumulation were 20 mg/kg for rat, 24 mg/kg for guinea pig and 30 mg/kg for rabbit. These data indicate that SC-41930 is effective locally to prevent acute colonic inflammation.

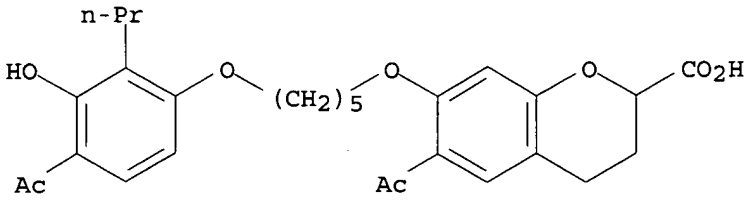
L3 ANSWER 86 OF 101 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:19015 CAPLUS
DOCUMENT NUMBER: 114:19015
TITLE: Studies on the role of leukotrienes in murine allergic and irritant contact dermatitis
AUTHOR(S): Rosenbach, T.; Csato, M.; Czarnetzki, B. M.
CORPORATE SOURCE: Dep. Dermatol., Univ. Clin., Muenster, Fed. Rep. Ger.
SOURCE: British Journal of Dermatology (1988), 118(1), 1-6
CODEN: BJDEAZ; ISSN: 0007-0963
DOCUMENT TYPE: Journal
LANGUAGE: English

IT **131147-29-0**, Ro 23-3544
RL: BIOL (Biological study)
(allergic and irritant contact dermatitis response to, peptidoleukotrienes in relation to)
RN 131147-29-0 CAPLUS
AB A specific peptidoleukotriene receptor antagonist, Ro 23-3544, was tested for its efficacy in modulating DNFB-induced allergic and croton oil-induced irritant contact dermatitis in mouse ears. Treatment shortly after elicitation of the dermatitis, and for up to 5 days thereafter, was moderately effective in suppressing DNFB-induced ear swelling in a dose-dependent fashion. Daily pretreatment of the ears for 1 wk caused a more marked redn. of DNFB-induced ear swelling during the first 48 h after elicitation. No redn., but rather an increase in ear swelling was obsd. with croton oil-induced dermatitis. Thus, peptidoleukotrienes play a role in the early stages of elicitation of murine allergic, but not irritant contact dermatitis and a specific receptor antagonist can partially reverse the effect of peptidoleukotrienes once the dermatitis is established.

L3 ANSWER 87 OF 101 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1990:478166 CAPLUS
DOCUMENT NUMBER: 113:78166
TITLE: Preparation of 7-(phenoxypentyloxy)-2-dihydrobenzopyranyl alkanoates and analogs as antiallergic agents
INVENTOR(S): Manchand, Percy Sarwood; Micheli, Robert Angelo
PATENT ASSIGNEE(S): Hoffmann-La Roche, F., und Co. A.-G., Switz.
SOURCE: Eur. Pat. Appl., 15 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

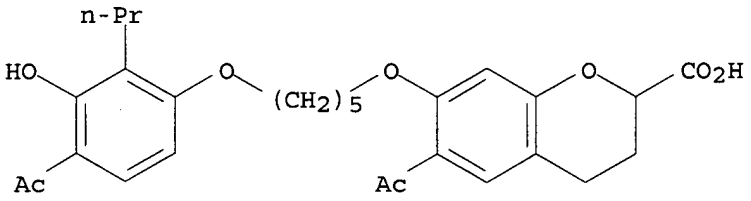
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 355617	A1	19900228	EP 1989-114880	19890811
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
US 4931574	A	19900605	US 1988-235129	19880823
ZA 8906332	A	19900530	ZA 1989-6332	19890818
DK 8904132	A	19900224	DK 1989-4132	19890822
JP 02108684	A2	19900420	JP 1989-214251	19890822
AU 8940166	A1	19900301	AU 1989-40166	19890823
AU 616997	B2	19911114		
US 5003090	A	19910326	US 1990-495527	19900319

PRIORITY APPLN. INFO.: US 1988-235129 19880823
OTHER SOURCE(S): MARPAT 113:78166
IT **96565-55-8P 96566-25-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as antiallergic agent)
RN 96565-55-8 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 6-acetyl-7-[[5-(4-acetyl-3-hydroxy-2-propylphenoxy)pentyl]oxy]-3,4-dihydro-, monosodium salt (9CI) (CA INDEX NAME)



● Na

RN 96566-25-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 6-acetyl-7-[[5-(4-acetyl-3-hydroxy-2-propylphenoxy)pentyl]oxy]-3,4-dihydro- (9CI) (CA INDEX NAME)



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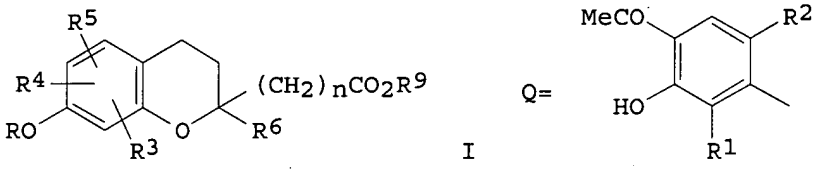

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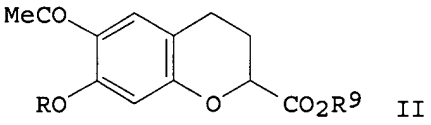


II

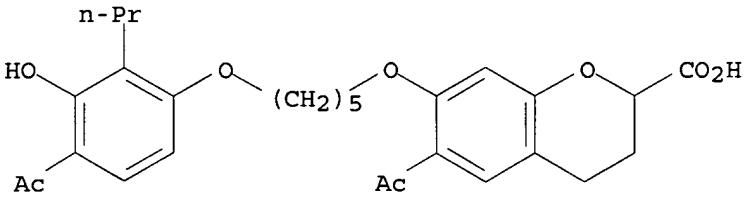
AB The title compds. [I; R = QO(CH2)5; R1 = H, alkyl; R2 = H, halo; R3-R5 = H, acyl, alkyl; R6 = H, alkyl; R9 = H, cation; n = 0-4] were prepd. as antiallergic agents (no data). Thus, bezopyrancarboxylate II)R = H, R9 = Me) was stirred 19 h with AcO(CH2)5Br (prepn. given) in DMSO contg. K2Co3 and the product converted in 2 steps to II [R = MeSO2O(CH2)5, R9 = Me] which was refluxed 6.5 h with QOH (R1 = R2 = H) in PhMe contg. K2CO3 and (MeOCH2CH2OCH2CH2)3N to give, after sapon., II [R = QO(CH2)5, R1 = R2 = H, R9 = Na].

L3 ANSWER 88 OF 101 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1990:216695 CAPLUS
DOCUMENT NUMBER: 112:216695
TITLE: Preparation and formulation of phenoxyalkoxy-3,4-dihydro-2H-1-benzopyrans for therapy of allergic and inflammatory disorders
INVENTOR(S): Laurenzano, Anthony James; Partridge, John Joseph
PATENT ASSIGNEE(S): Hoffmann-La Roche, F., und Co. A.-G., Switz.
SOURCE: Eur. Pat. Appl., 31 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

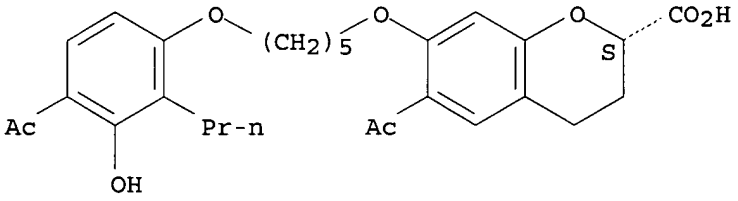
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 336068	A1	19891011	EP 1989-101886	19890203
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
DK 8900596	A	19890812	DK 1989-596	19890209
JP 01246275	A2	19891002	JP 1989-28803	19890209
ZA 8901036	A	19891025	ZA 1989-1036	19890209
AU 8929820	A1	19890817	AU 1989-29820	19890210

PRIORITY APPLN. INFO.: US 1988-154765 19880211
OTHER SOURCE(S): MARPAT 112:216695
IT **96566-25-5 96686-71-4 96686-73-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(esterification of)
RN 96566-25-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 6-acetyl-7-[[5-(4-acetyl-3-hydroxy-2-propylphenoxy)pentyl]oxy]-3,4-dihydro- (9CI) (CA INDEX NAME)



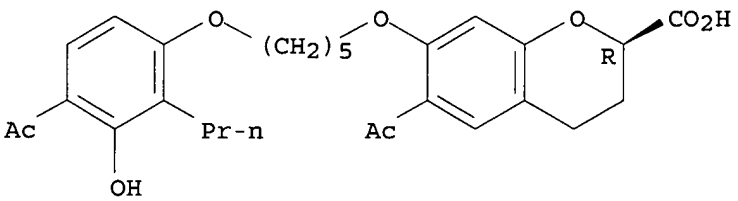
RN 96686-71-4 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 6-acetyl-7-[[5-(4-acetyl-3-hydroxy-2-propylphenoxy)pentyl]oxy]-3,4-dihydro-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 96686-73-6 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 6-acetyl-7-[[5-(4-acetyl-3-hydroxy-2-propylphenoxy)pentyl]oxy]-3,4-dihydro-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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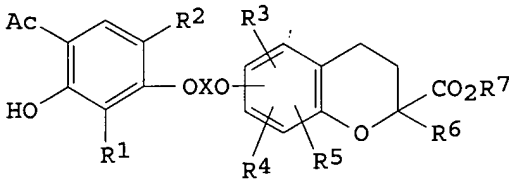
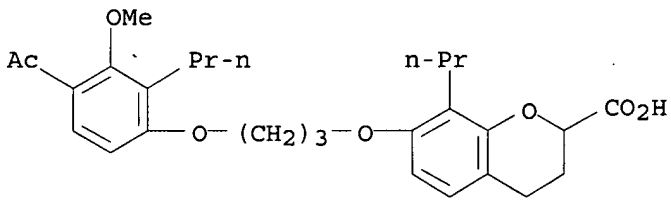


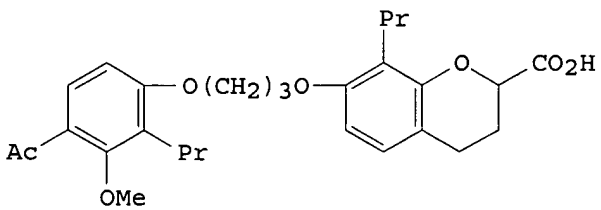
I

AB Title compds. I (R1, R6 = H, alkyl; R2 = H, halo; R3-R5 = H, acyl, alkyl provided only 1 group is acyl; R7 = higher alkyl, PhCH2; X = C3-7 alkylene) and their enantiomers were prepd. and formulated. Thus, (.+-.)-6-acetyl-7-[5-(4-acetyl-3-hydroxy-2-propylphenoxy)pentyloxy]-3,4-dihydro-2H-1-benzopyran-2-carboxylic acid (II) was esterified by 1-octanol in PhMe with p-MeC6H4SO3H.H2O catalyst under Dean-Stark conditions to give II n-octyl ester (III) in 75% yield. Tablets contg. III, lactose, starch, polyvinylpyrrolidone, and Mg stearate were prepd. and coated with a soln. of hydroxypropyl methylcellulose phthalate in alc.-CH2Cl2. Seven syntheses and 11 formulations are described.

L3 ANSWER 89 OF 101 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1990:111716 CAPLUS
DOCUMENT NUMBER: 112:111716
TITLE: SC-41930 inhibits neutrophil infiltration of the cavine dermis induced by 12(R)-hydroxyeicosatetraenoic acid
AUTHOR(S): Fretland, D. J.; Widomski, D. L.; Shone, R. L.; Penning, T. D.; Miyashiro, J. M.; Djuric, S. W.
CORPORATE SOURCE: Gastrointest. Dis. Res. Dep., G. D. Searle and Co., Skokie, IL, 60077, USA
SOURCE: Prostaglandins, Leukotrienes and Essential Fatty Acids (1989), 38(3), 169-72
CODEN: PLEAEU; ISSN: 0952-3278
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **120072-59-5**, SC-41930
RL: BIOL (Biological study)
(neutrophil infiltration inhibition by, psoriasis in relation to)
RN 120072-59-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



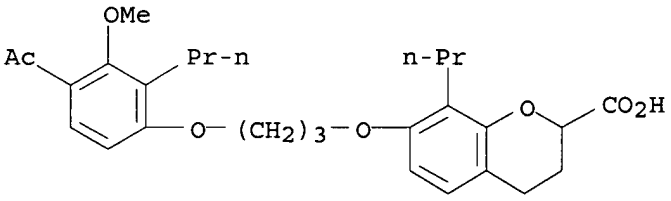
GI



I

AB Psoriasis is a disease state characterized by epidermal proliferation, neutrophil infiltration, and release of the proinflammatory mediators leukotriene-B4 (LTB4) and 12(R)-hydroxyeicosatetraenoic acid [12(R)-HETE]. LTB4 and 12(R)-HETE are chemoattractant to the neutrophil, the latter approx. 1000-fold less potent. LTB4 and 12(R)-HETE are present in psoriatic scale, the latter in quantities so much greater than LTB4 that it is proposed as a primary mediator of neutrophil infiltration in psoriasis. 12(R)-HETE, synthesized in optically pure form by a new, shorter route, was injected into the cavine dermis. At a dose of 25 .mu.g per intradermal site, 12(R)-HETE was a significant chemoattractant to the neutrophil (as assessed by dermal myeloperoxidase levels). SC-41930 (I), given intragastrically, inhibited 12(R)-HETE-induced neutrophil infiltration of the cavine dermis with an ED50 value of 13.5 mg/kg. Compds. such as SC-41930 may have utility for treating human psoriasis.

L3 ANSWER 90 OF 101 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1990:92485 CAPLUS
DOCUMENT NUMBER: 112:92485
TITLE: SC-41930: an inhibitor of leukotriene B4-stimulated human neutrophil functions
AUTHOR(S): Tsai, B. S.; Villani-Price, D.; Keith, R. H.; Zemaitis, J. M.; Bauer, R. F.; Leonard, R.; Djuric, S. W.; Shone, R. L.
CORPORATE SOURCE: Gastrointest. Dis. Res., G. D. Searle and Co., Skokie, IL, 60077, USA
SOURCE: Prostaglandins (1989), 38(6), 655-74
CODEN: PRGLBA; ISSN: 0090-6980
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **120072-59-5**, SC 41930
RL: BIOL (Biological study)
(neutrophil of human functions inhibition by)
RN 120072-59-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



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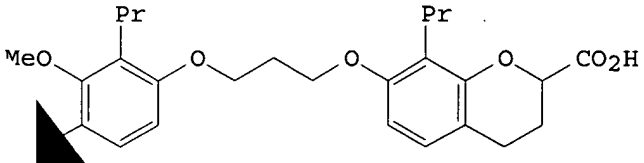
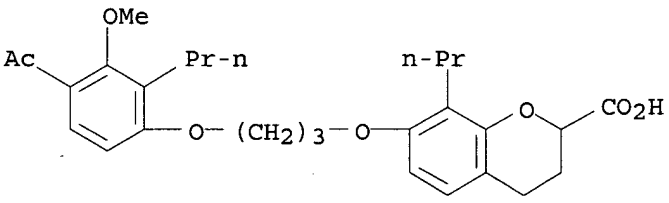


I

oncns. up to 100 .mu.M, SC-41930 (I) alone exhibited no effect on neutrophil migration, but it dose-dependently inhibited neutrophil xis induced by leukotriene B4 (LTB4) in a modified Boyden chamber. -3 .mu.M competitively inhibited LTB4-induced chemotaxis with a of 6.35. Although inactive at 10 .mu.M against complement 5a

(C5a)-induced chemotaxis, I inhibited N-formyl-methionyl-leucyl-phenylalanine (fMLP)-induced chemotaxis (with 10 times less potency than against LTB4-induced chemotaxis). I inhibited [3H]LTB4 and [3H]fMLP binding to their receptor sites on human neutrophils with KD values of 0.2 .mu.M and 2 .mu.M, resp. I also inhibited neutrophil chemotaxis induced by 20-hydroxy-LTB4 or 12(R)-HETE. At concns. up to 10 .mu.M, I alone did not cause neutrophil degranulation, but it inhibited LTB4-induced degranulation in a noncompetitive manner. I also inhibited fMLP- or C5a-induced degranulation, but was about 8 and 10 times less effective for fMLP and C5a, resp. Thus, I is a human neutrophil LTB4 receptor antagonist with greater specificity for LTB4 than for fMLP or C5a receptors.

L3 ANSWER 91 OF 101 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1989:624967 CAPLUS
DOCUMENT NUMBER: 111:224967
TITLE: Effect of a leukotriene B4 receptor antagonist on leukotriene B4-induced neutrophil chemotaxis in cavine dermis
AUTHOR(S): Fretland, D. J.; Widomski, D. L.; Zemaitis, J. M.; Djuric, S. W.; Shone, R. L.
CORPORATE SOURCE: Dep. Gastrointest. Res., G. D. Searle and Co., Skokie, IL, 60077, USA
SOURCE: Inflammation (New York, NY, United States) (1989), 13(5), 601-5
CODEN: INFLD4; ISSN: 0360-3997
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **120072-59-5**, SC 41930
RL: BIOL (Biological study)
(LTB4-induced neutrophil chemotaxis in dermis response to, inflammation inhibition in relation to)
RN 120072-59-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)

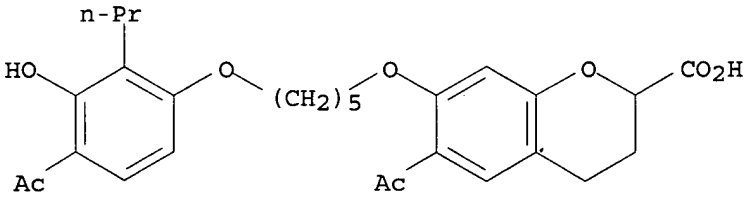


AB Leukotriene B4 (LTB4) is a proinflammatory product of arachidonic acid metab. that has been implicated as a mediator in a no. of inflammatory diseases. When injected intradermally into the cavine, LTB4 elicites a dose-dependent immigration (chemotaxis) of neutrophils (PMNs) into the injection sites as assessed by the presence of a neutrophil marker enzyme myeloperoxidase. SC-41930, a potent LTB4 receptor antagonist inhibited the chemotactic actions of LTB4 when coadministered into the dermal site and when given i.v. or orally with ED50 values of 200 ng, 0.5 mg/kg, and 0.6 mg/kg resp. This compd. may well have application in disease states, such as inflammatory bowel disease and psoriasis, where LTB4 is implicated as a proinflammatory mediator.

L3 ANSWER 92 OF 101 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1989:553565 CAPLUS
DOCUMENT NUMBER: 111:153565
TITLE: 3,4-Dihydro-2H-1-benzopyran-2-carboxylic acids and related compounds as leukotriene antagonists
AUTHOR(S): Cohen, Noal; Weber, Giuseppe; Banner, Bruce L.;

Lopresti, Rocco J.; Schaer, Beatrice; Focella, Antonino; Zenchoff, Gladys B.; Chiu, Anne Marie; Todaro, Louis; et al.
CORPORATE SOURCE: Roche Res. Cent., Hoffmann-La Roche Inc., Nutley, NJ, 07110, USA
SOURCE: Journal of Medicinal Chemistry (1989), 32(8), 1842-60
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 111:153565

IT **96565-55-8**
RL: RCT (Reactant); RACT (Reactant or reagent)
(oxidn. of, with potassium persulfate)
RN 96565-55-8 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 6-acetyl-7-[[5-(4-acetyl-3-hydroxy-2-propylphenoxy)pentyl]oxy]-3,4-dihydro-, monosodium salt (9CI) (CA INDEX NAME)



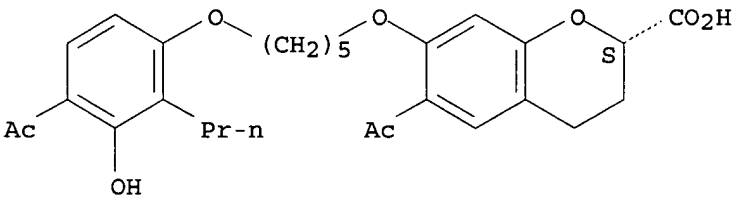
● Na

IT **96686-72-5P**
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and crystal structure of)
RN 96686-72-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 6-acetyl-7-[[5-(4-acetyl-3-hydroxy-2-propylphenoxy)pentyl]oxy]-3,4-dihydro-, (S)-, compd. with (R)-.alpha.-methylbenzenemethanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 96686-71-4
CMF C28 H34 O8

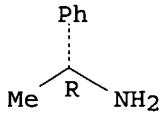
Absolute stereochemistry.



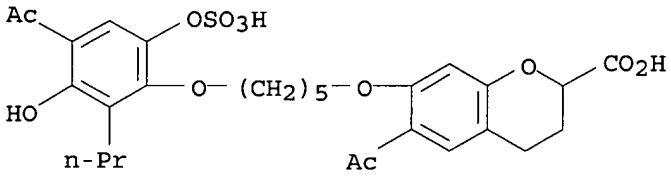
CM 2

CRN 3886-69-9
CMF C8 H11 N

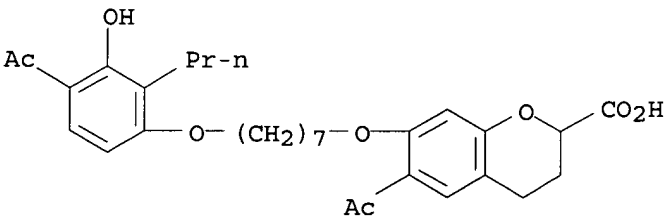
Absolute stereochemistry.



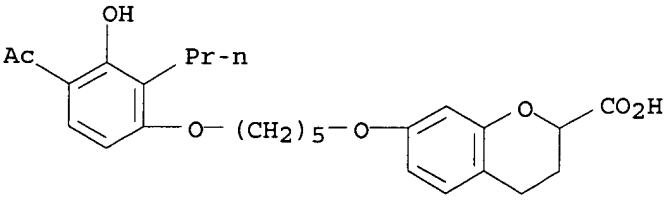
IT **122444-33-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and esterification of)
RN 122444-33-1 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 6-acetyl-7-[[5-[4-acetyl-3-hydroxy-2-propyl-6-(sulfooxy)phenoxy]pentyl]oxy]-3,4-dihydro- (9CI) (CA INDEX NAME)



IT **96566-26-6P 96566-45-9P 96566-60-8P**
96566-63-1P 96566-65-3P 96566-66-4P
96566-69-7P 96594-21-7P 96686-71-4P
96686-73-6P 122444-06-8P 122444-07-9P
122444-08-0P 122444-10-4P 122444-12-6P
122444-13-7P 122444-16-0P 122444-17-1P
122444-18-2P 122444-19-3P 122444-20-6P
122444-21-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and leukotriene antagonists activity of)
RN 96566-26-6 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 6-acetyl-7-[[7-(4-acetyl-3-hydroxy-2-propylphenoxy)heptyl]oxy]-3,4-dihydro- (9CI) (CA INDEX NAME)

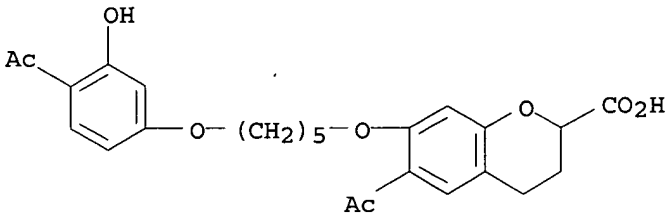


RN 96566-45-9 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[[5-(4-acetyl-3-hydroxy-2-propylphenoxy)pentyl]oxy]-3,4-dihydro- (9CI) (CA INDEX NAME)

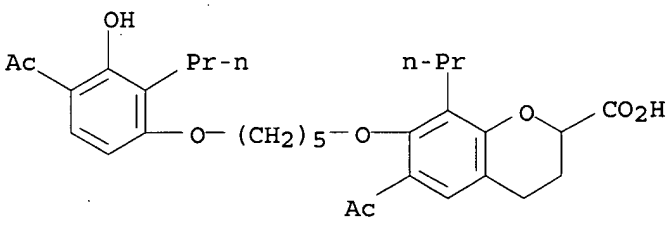


RN 96566-60-8 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 6-acetyl-7-[[5-(4-acetyl-3-

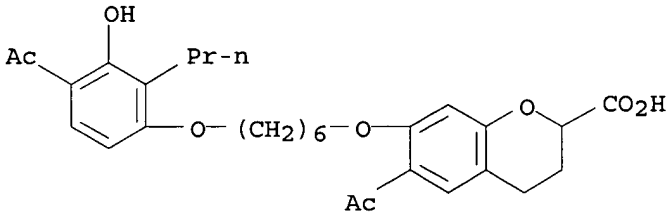
hydroxyphenoxy)pentyl]oxy]-3,4-dihydro- (9CI) (CA INDEX NAME)



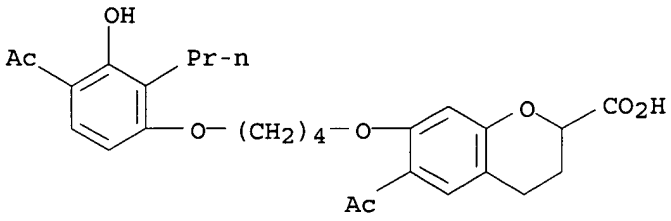
RN 96566-63-1 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 6-acetyl-7-[[5-(4-acetyl-3-hydroxy-2-propylphenoxy)pentyl]oxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



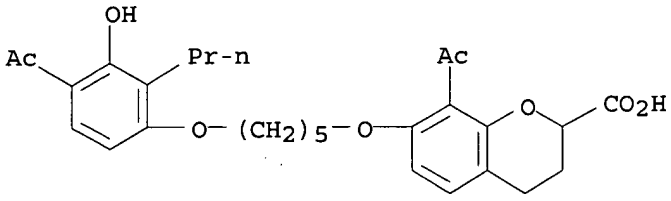
RN 96566-65-3 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 6-acetyl-7-[[6-(4-acetyl-3-hydroxy-2-propylphenoxy)hexyl]oxy]-3,4-dihydro- (9CI) (CA INDEX NAME)



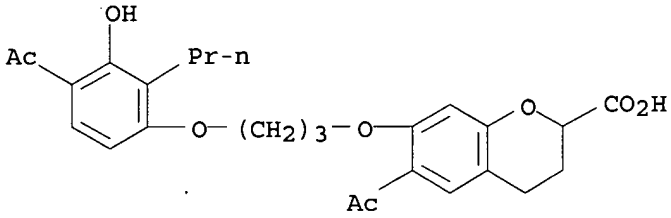
RN 96566-66-4 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 6-acetyl-7-[4-(4-acetyl-3-hydroxy-2-propylphenoxy)butoxy]-3,4-dihydro- (9CI) (CA INDEX NAME)



RN 96566-69-7 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 8-acetyl-7-[[5-(4-acetyl-3-hydroxy-2-propylphenoxy)pentyl]oxy]-3,4-dihydro- (9CI) (CA INDEX NAME)

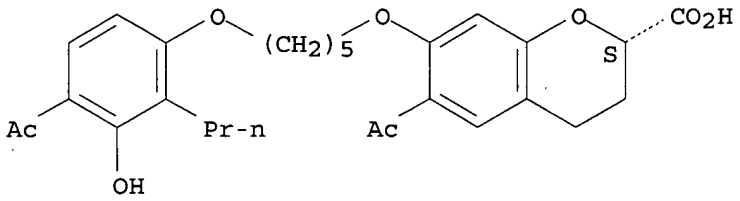


RN 96594-21-7. CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 6-acetyl-7-[3-(4-acetyl-3-hydroxy-2-propylphenoxy)propoxy]-3,4-dihydro- (9CI) (CA INDEX NAME)



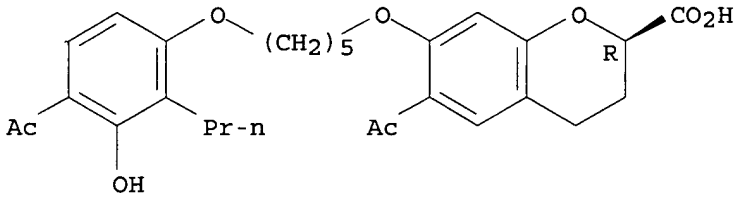
RN 96686-71-4 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 6-acetyl-7-[[5-(4-acetyl-3-hydroxy-2-propylphenoxy)pentyl]oxy]-3,4-dihydro-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

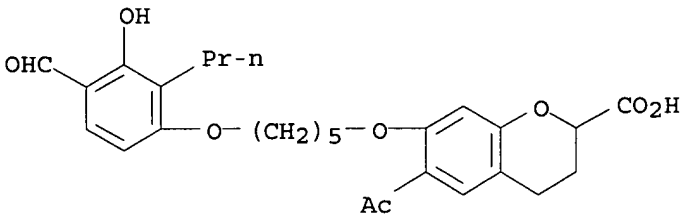


RN 96686-73-6 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 6-acetyl-7-[[5-(4-acetyl-3-hydroxy-2-propylphenoxy)pentyl]oxy]-3,4-dihydro-, (R)- (9CI) (CA INDEX NAME)

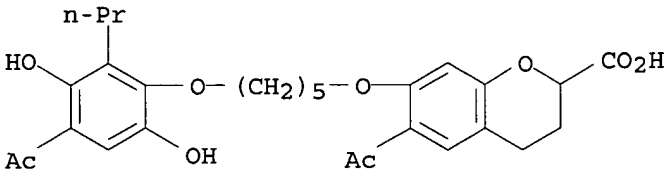
Absolute stereochemistry.



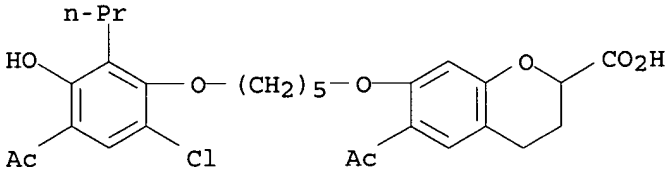
RN 122444-06-8 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 6-acetyl-7-[[5-(4-formyl-3-hydroxy-2-propylphenoxy)pentyl]oxy]-3,4-dihydro- (9CI) (CA INDEX NAME)



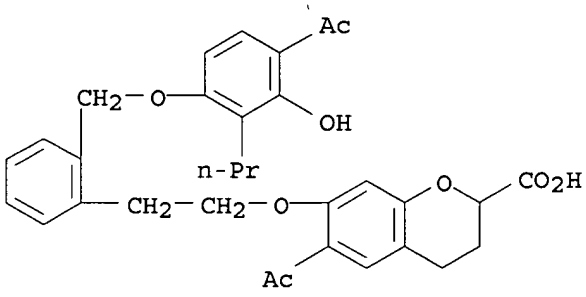
RN 122444-07-9 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 6-acetyl-7-[[5-(4-acetyl-3,6-dihydroxy-2-propylphenoxy)pentyl]oxy]-3,4-dihydro- (9CI) (CA INDEX NAME)



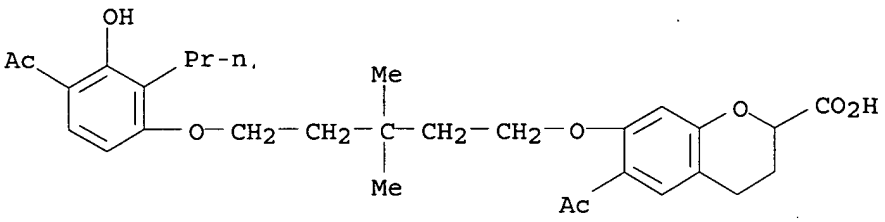
RN 122444-08-0 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 6-acetyl-7-[[5-(4-acetyl-6-chloro-3-hydroxy-2-propylphenoxy)pentyl]oxy]-3,4-dihydro- (9CI) (CA INDEX NAME)



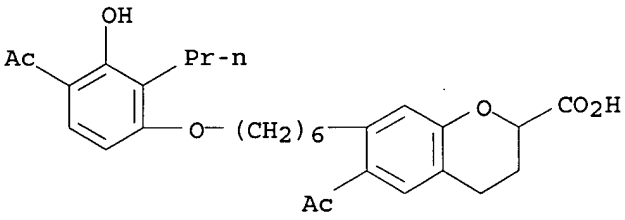
RN 122444-10-4 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 6-acetyl-7-[2-[2-[(4-acetyl-3-hydroxy-2-propylphenoxy)methyl]phenyl]ethoxy]-3,4-dihydro- (9CI) (CA INDEX NAME)



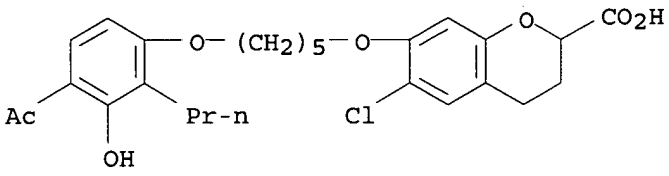
RN 122444-12-6 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 6-acetyl-7-[[5-(4-acetyl-3-hydroxy-2-propylphenoxy)-3,3-dimethylpentyl]oxy]-3,4-dihydro- (9CI) (CA INDEX NAME)



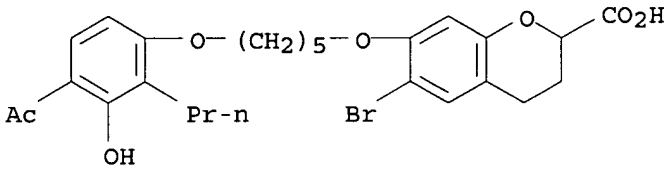
RN 122444-13-7 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 6-acetyl-7-[6-(4-acetyl-3-hydroxy-2-propylphenoxy)hexyl]-3,4-dihydro- (9CI) (CA INDEX NAME)



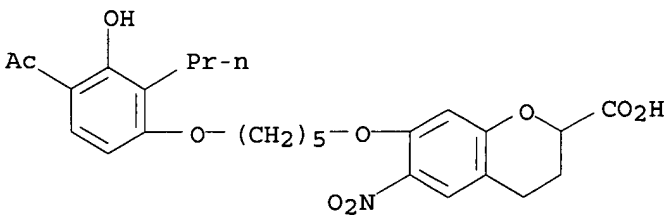
RN 122444-16-0 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[[5-(4-acetyl-3-hydroxy-2-propylphenoxy)pentyl]oxy]-6-chloro-3,4-dihydro- (9CI) (CA INDEX NAME)

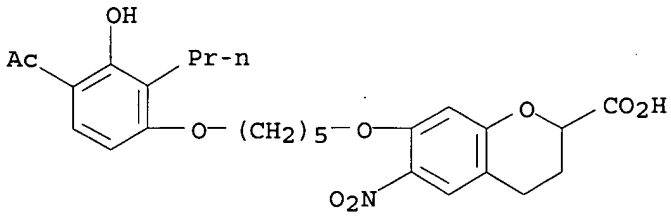


RN 122444-17-1 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[[5-(4-acetyl-3-hydroxy-2-propylphenoxy)pentyl]oxy]-6-bromo-3,4-dihydro- (9CI) (CA INDEX NAME)

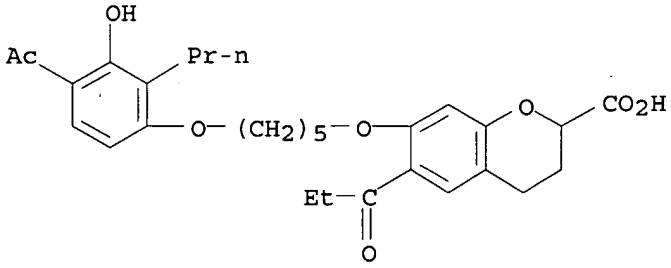


RN 122444-18-2 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[[5-(4-acetyl-3-hydroxy-2-propylphenoxy)pentyl]oxy]-3,4-dihydro-6-nitro- (9CI) (CA INDEX NAME)

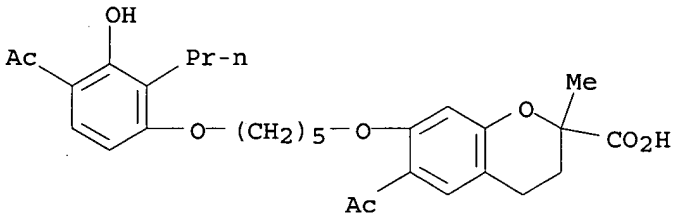




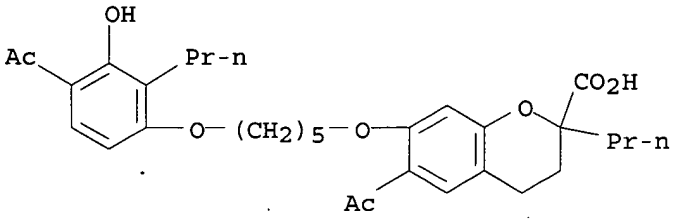
RN 122444-19-3 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[[5-(4-acetyl-3-hydroxy-2-propylphenoxy)pentyl]oxy]-3,4-dihydro-6-(1-oxopropyl)- (9CI) (CA INDEX NAME)



RN 122444-20-6 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 6-acetyl-7-[[5-(4-acetyl-3-hydroxy-2-propylphenoxy)pentyl]oxy]-3,4-dihydro-2-methyl- (9CI) (CA INDEX NAME)



RN 122444-21-7 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 6-acetyl-7-[[5-(4-acetyl-3-hydroxy-2-propylphenoxy)pentyl]oxy]-3,4-dihydro-2-propyl- (9CI) (CA INDEX NAME)



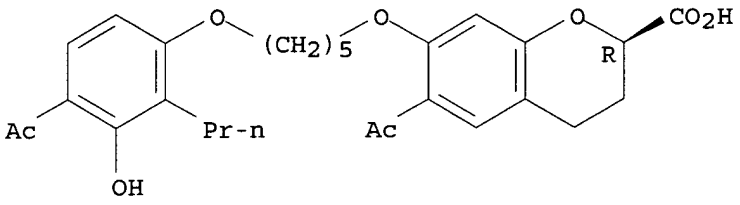
IT **122444-41-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 122444-41-1 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 6-acetyl-7-[[5-(4-acetyl-3-hydroxy-2-propylphenoxy)pentyl]oxy]-3,4-dihydro-, (R)-, compd. with

(S)-.alpha.-methylbenzenemethanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 96686-73-6
CMF C28 H34 O8

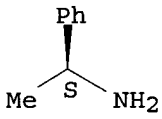
Absolute stereochemistry.



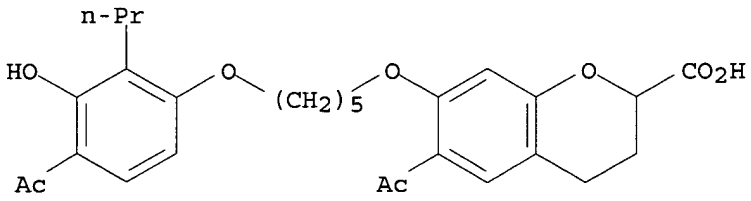
CM 2

CRN 2627-86-3
CMF C8 H11 N

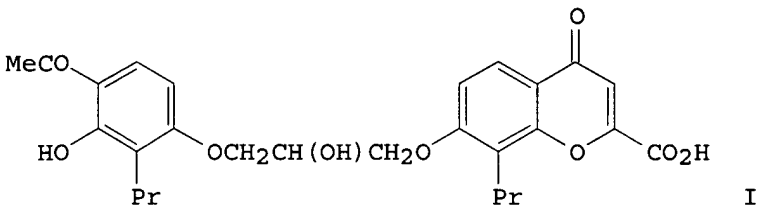
Absolute stereochemistry.



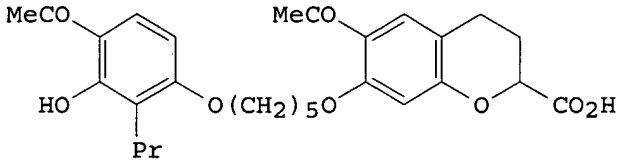
IT **96566-25-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn., resoln., and leukotriene antagonist activity of)
RN 96566-25-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 6-acetyl-7-[[5-(4-acetyl-3-hydroxy-2-propylphenoxy)pentyl]oxy]-3,4-dihydro- (9CI) (CA INDEX NAME)



GI



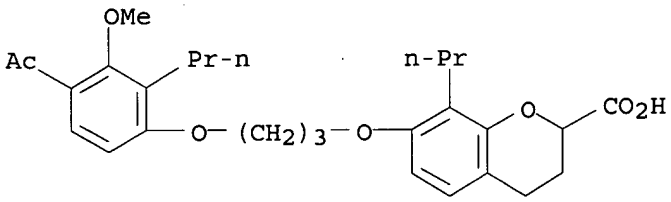
I



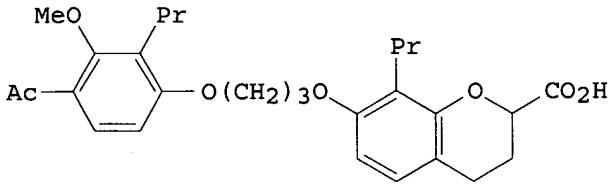
II

AB Evaluation of a series of 3,4-dihydro-2H-1-benzopyran-2-carboxylic acids linked to the 2-hydroxyacetophenone pharmacophore present in the std. peptidoleukotriene antagonist FPL 55712 (I) has led to the discovery of Ro 23-3544 (II), an antagonist possessing greater potency and duration of action vs LTD4 than the std. (aerosol route of administration, guinea pig bronchoconstriction model). Interestingly, II also potently inhibited bronchoconstriction induced by LTB4 whereas I did not. Attempts to establish structure-activity relationships in this series involved modifications in the 2-hydroxyacetophenone moiety, the linking chain, and the chroman system. All variations produced analogs which were either inactive or possessed reduced potency relative to II. Optical resoln. of II was achieved by two methods. Abs. configurations of the enantiomers were detd. via x-ray crystallog. analyses of an intermediate as well as a salt of the S enantiomer. Although the enantiomers exhibited similar potencies in in vitro assays and in vivo when administered i.v., significant differences were obsd. in the guinea pig bronchoconstriction model vs LTC4 and LTD4 when administered by the aerosol route (S-antipode 15-fold more potent). The properties of II were compared with several recently reported leukotriene antagonists.

L3 ANSWER 93 OF 101 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1989:433445 CAPLUS
DOCUMENT NUMBER: 111:33445
TITLE: The effect of leukotriene-B4 receptor antagonist, SC-41930, on acetic acid-induced colonic inflammation
AUTHOR(S): Fretland, D. J.; Levin, S.; Tsai, B. S.; Djuric, S. W.; Widomski, D. L.; Zemaitis, J. M.; Shone, R. L.; Bauer, R. F.
CORPORATE SOURCE: Dep. Gastrointest. Dis. Res., G. D. Searle and Co., Skokie, IL, 60077, USA
SOURCE: Agents and Actions (1989), 27(3-4), 395-7
CODEN: AGACBH; ISSN: 0065-4299
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **120072-59-5**, SC 41930
RL: BIOL (Biological study)
(intestinal inflammation therapy with, as LTB4 receptor antagonist)
RN 120072-59-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



GI



I

AB SC 41930 (I) is a potent in vitro LTB4 receptor antagonist. LTB4 levels are elevated in colonic tissue of inflammatory bowel disease (IBD) patients, which may account for the high degree of neutrophil (PMN) infiltration. The guinea pig acetic acid-induced colonic inflammation model has characteristics of IBD including PMN infiltration, edema, ulceration and necrosis. The model was used to evaluate the effect of SC-41930. SC-41930 was given orally, 30 min before and after intrarectal administration of 3% acetic acid. The PMN marker enzyme, myeloperoxidase, was measured along with histol. evaluation to assess inflammation. Both parameters showed significantly less inflammation in SC-41930 treated animals with an oral ED50 of 20 mg/kg. These study results indicate a role for LTB4 in colonic inflammation and that an LTB4 receptor antagonist may be beneficial for treatment of IBD.

L3 ANSWER 94 OF 101 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1989:231387 CAPLUS
DOCUMENT NUMBER: 110:231387

TITLE: 7-[3-(4-Acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl-2H-1-benzopyran-2-carboxylic acid: an orally active selective leukotriene B4 receptor antagonist

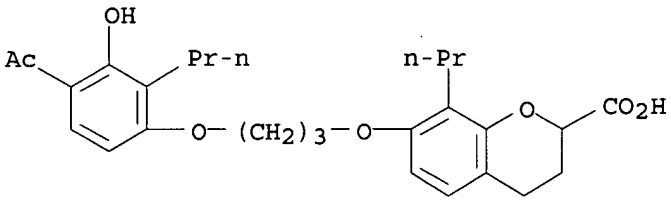
AUTHOR(S): Djuric, Stevan W.; Collins, Paul W.; Jones, Peter H.; Shone, Robert L.; Tsai, Bie Shung; Fretland, Donald J.; Butchko, Gregory M.; Villani-Price, Doreen; Keith, Robert H.; et al.
CORPORATE SOURCE: Gastrointest. Dis. Res., G. D. Searle and Co., Skokie, IL, 60077, USA

SOURCE: Journal of Medicinal Chemistry (1989), 32(6), 1145-7
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 110:231387

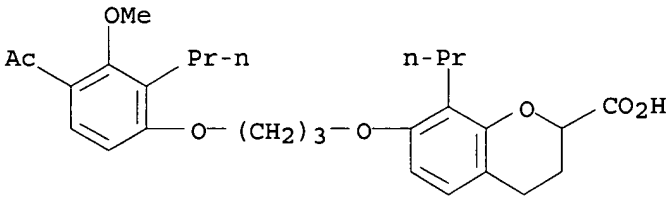
IT **99453-98-2**
RL: RCT (Reactant); RACT (Reactant or reagent)
(leukotriene B4 receptor antagonistic activity of)

RN 99453-98-2 CAPLUS

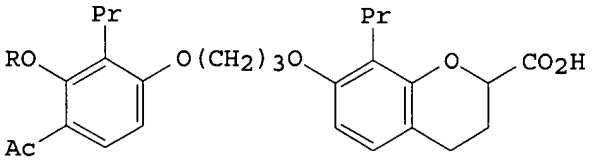
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-3-hydroxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



IT **120072-59-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and leukotriene B4 receptor antagonistic activity of)
RN 120072-59-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



GI



I

AB The title compd., (I, R = Me) (II), was prepd. by sequential coupling of the two arom. groups with Cl(CH2)3Br. II is the first orally active, selective leukotriene B4 receptor antagonist. Related compd. I (R = H) did not show any receptor antagonistic activity.

L3 ANSWER 95 OF 101 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1989:199191 CAPLUS
DOCUMENT NUMBER: 110:199191
TITLE: Preparation of 6-acetyl-7-[5-(4-acetyl-3-hydroxy-2-propylphenoxy)pentyloxy]-3,4-dihydro-2H-1-benzopyran-2-carboxylates and antiinflammatory pharmaceuticals containing them
INVENTOR(S): Gaginella, Timothy Samuel; Welton, Ann Frances; Will, Peter Graig
PATENT ASSIGNEE(S): Hoffmann-La Roche, F., und Co. A.-G., Switz.
SOURCE: Eur. Pat. Appl., 29 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 256532	A1	19880224	EP 1987-111781	19870813
EP 256532	B1	19920520		

R: BE, CH, DE, FR, GB, IT, LI, LU, NL, SE

ZA 8705319	A	19880427	ZA 1987-5319	19870720
IL 83533	A1	19911121	IL 1987-83533	19870813
AU 8777140	A1	19880218	AU 1987-77140	19870814
AU 607931	B2	19910321		
JP 63048216	A2	19880229	JP 1987-201953	19870814
HU 46845	A2	19881228	HU 1987-3669	19870814
HU 203471	B	19910828		
CA 1303508	A1	19920616	CA 1987-544521	19870814
US 5112856	A	19920512	US 1990-569241	19900816

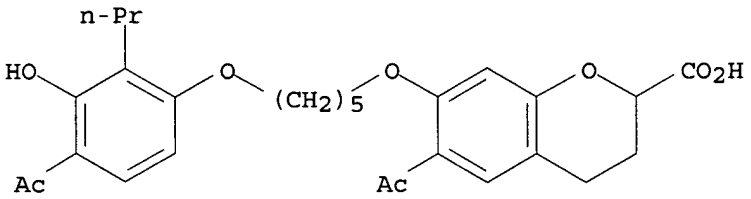
PRIORITY APPLN. INFO.: US 1986-897450 19860815
US 1989-315014 19890224

OTHER SOURCE(S): MARPAT 110:199191

IT **96565-55-8 96566-25-5**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceuticals contg., for treatment of enteritis)

RN 96565-55-8 CAPLUS

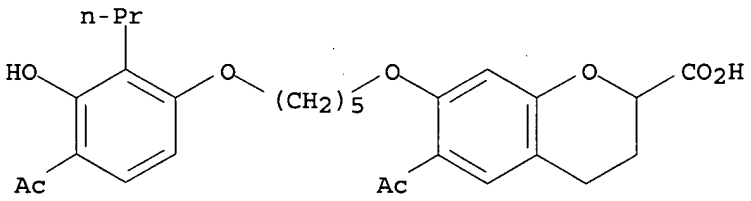
CN 2H-1-Benzopyran-2-carboxylic acid, 6-acetyl-7-[[5-(4-acetyl-3-hydroxy-2-propylphenoxy)pentyl]oxy]-3,4-dihydro-, monosodium salt (9CI) (CA INDEX NAME)



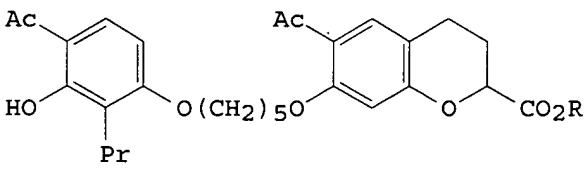
● Na

RN 96566-25-5 CAPLUS

CN 2H-1-Benzopyran-2-carboxylic acid, 6-acetyl-7-[[5-(4-acetyl-3-hydroxy-2-propylphenoxy)pentyl]oxy]-3,4-dihydro- (9CI) (CA INDEX NAME)



GI



I

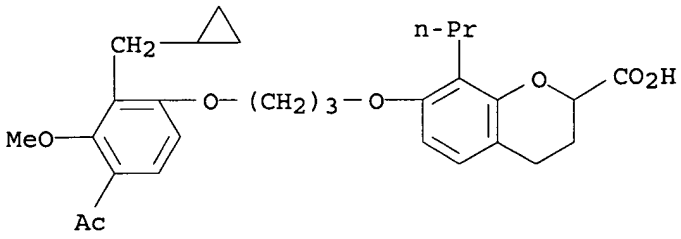
AB The title dihydrobenzopyran derivs. (I; R = H, lower alkyl), their enantiomeric forms, or their salts are inflammation inhibitors for enteritis and other forms of inflammation of the intestinal mucosa assocd.

with the presence of leukotriene. A mixt. of 20.2 g Me (.+-.)-6-acetyl-7-(5-bromopentyloxy)-3,4-dihydro-2H-1-benzopyran-2-carboxylate and 11.0 g 2,4-dihydroxy-3-propylacetophenone were treated with 25.4 g K2CO3 in 436 mL dry Me2CO and 218 mL DMF for 5.5 h under reflux to give (.+-.)-I (R = Me) in 96.8% yield. Clindamycin-induced colitis in hamsters was characterized by edema, bleeding and stagnating blood flow, necrosis and mucosal erosions in the cecum and to a lesser extend in the colon. This condition was improved when the animals were treated with 100 mg/kg (.+-.)-I (R = H) and the hazard ratio (survival rate of treated vs. nontreated controls) was 64.0. Tablets contained (.+-.)-I (R = H) 100, lactose 30, preglatinized starch 4, microcryst. cellulose 20, modified starch 5, and Mg stearate 1 mg.

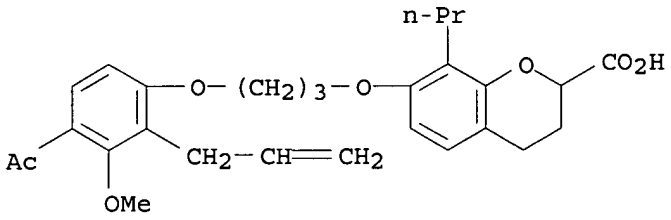
L3 ANSWER 96 OF 101 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1989:173088 CAPLUS
DOCUMENT NUMBER: 110:173088
TITLE: Preparation of alkoxy-substituted dihydrobenzopyran-2-carboxylates and analogs as antiinflammatory agents
INVENTOR(S): Djuric, Stevan Wakefield; Shone, Robert Larry; Yu, Stella Siu Tzyy
PATENT ASSIGNEE(S): Searle, G. D., and Co., USA
SOURCE: Eur. Pat. Appl., 56 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 292977	A1	19881130	EP 1988-108449	19880527
EP 292977	B1	19910904		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, NL, SE				
US 4889871	A	19891226	US 1988-188708	19880512
NO 8802317	A	19881130	NO 1988-2317	19880526
NO 171063	B	19921012		
NO 171063	C	19930120		
AU 8816681	A1	19881201	AU 1988-16681	19880526
AU 611153	B2	19910606		
IL 86502	A1	19940731	IL 1988-86502	19880526
CA 1337660	A1	19951128	CA 1988-567806	19880526
DK 8802901	A	19881130	DK 1988-2901	19880527
FI 8802505	A	19881130	FI 1988-2505	19880527
JP 01038045	A2	19890208	JP 1988-130037	19880527
JP 2758902	B2	19980528		
ZA 8803820	A	19890726	ZA 1988-3820	19880527
AT 66917	E	19910915	AT 1988-108449	19880527
ES 2051796	T3	19940701	ES 1988-108449	19880527

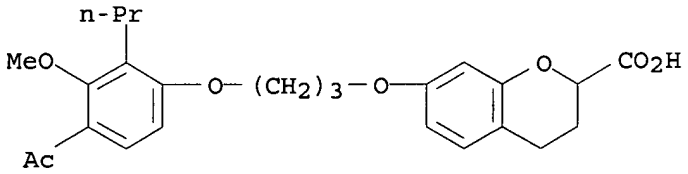
PRIORITY APPLN. INFO.: US 1987-57136 19870529
US 1988-188708 19880512
EP 1988-108449 19880527
OTHER SOURCE(S): CASREACT 110:173088; MARPAT 110:173088
IT **120072-38-0P 120072-40-4P 120072-41-5P 120072-50-6P 120072-54-0P 120072-56-2P 120072-59-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as antiinflammatory agent)
RN 120072-38-0 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[4-acetyl-2-(cyclopropylmethyl)-3-methoxyphenoxy]propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



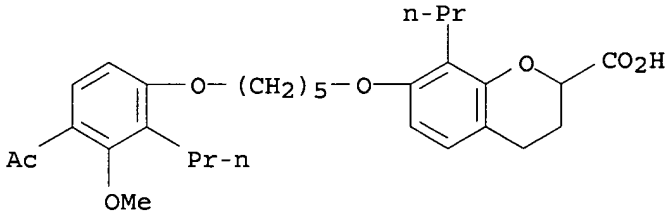
RN 120072-40-4 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[4-acetyl-3-methoxy-2-(2-propenyl)phenoxy]propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



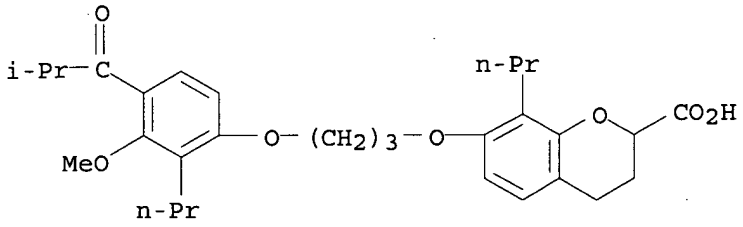
RN 120072-41-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro- (9CI) (CA INDEX NAME)



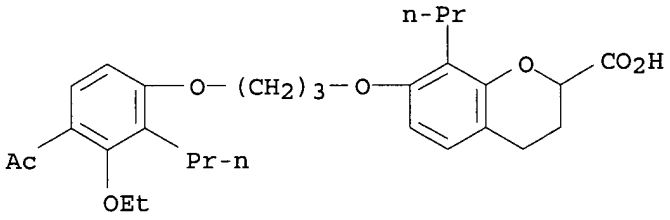
RN 120072-50-6 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[[5-(4-acetyl-3-methoxy-2-propylphenoxy)pentyl]oxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



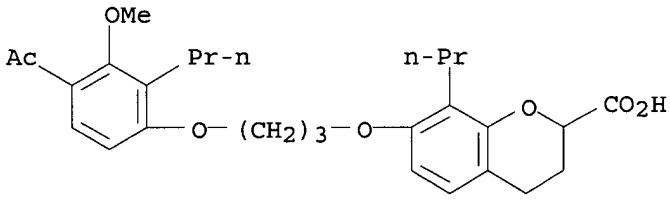
RN 120072-54-0 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 3,4-dihydro-7-[3-[3-methoxy-4-(2-methyl-1-oxopropyl)-2-propylphenoxy]propoxy]-8-propyl- (9CI) (CA INDEX NAME)



RN 120072-56-2 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-3-ethoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



RN 120072-59-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



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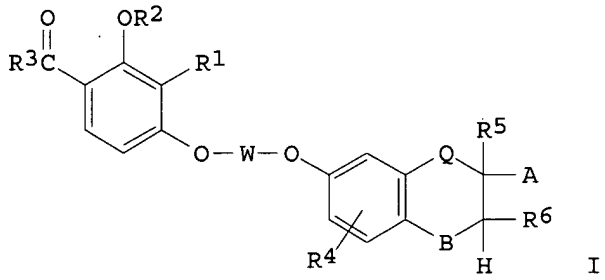

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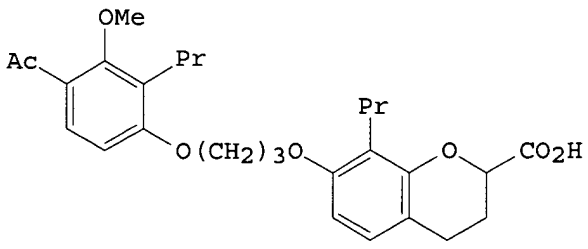
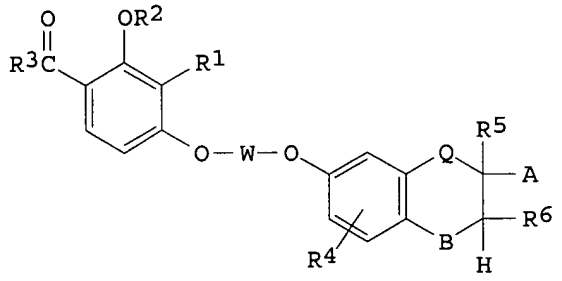
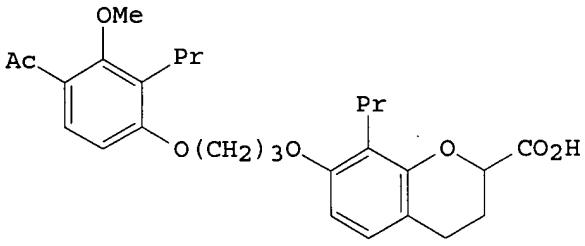


II



I



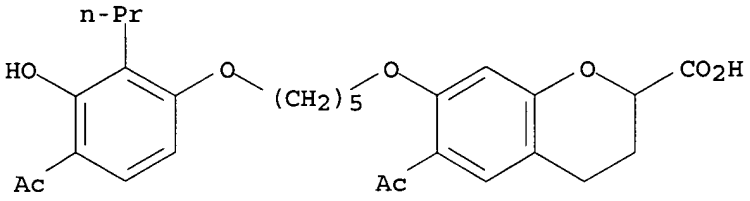
II

AB Title compds. I [R1 = C2-6 alkyl, alkenyl, or alkynyl, (CH2)nR; n = 1,2; R = C3-5 cycloalkyl; R2 = Me, Et; R3 = C1-5 alkyl; W = (CH2)x; C3-7 alkenylene or alkynylene, cyclopentanediyl; x = 2-7; R4 = H, C2-5 alkyl, alkenyl, or alkynyl; Q = O, CH2; B = CH2, CO, CHOH; R5 = H, C1-6 alkyl, C2-4 alkanoyl, CO2H, alkoxycarbonyl; (CH2)yCO2R8; R5R6 = bond; A = ZCO2R7, ZCONR9R10; Z = bond, C.ltoreq.6 alkylene or alkenylene; R7, R8 = H, C1-6 alkyl; y = 0-4; R9, R10 = H, C1-6 alkyl, C1-6 cycloalkyl; NR9R10 = heterocyclyl] were prepd. as antiinflammatory agents. Me 7-[3-(4-acetyl-3-hydroxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl-2H-1-benzopyran-2-carboxylate underwent etherification by MeI and K2CO3 in Me2CO, followed by sapon. with LiOH in aq. MeOH, to give (phenoxypropoxy)dihydrobenzopyrancarboxylic acid II. Compared to its prior art hydroxy analog II was 5-fold more potent as an LTB4 antagonist and over 10-fold less potent as an LTD4 antagonist.

L3 ANSWER 97 OF 101 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1989:33733 CAPLUS
DOCUMENT NUMBER: 110:33733
TITLE: Benzopyran derivatives as antiinflammatory agents
PATENT ASSIGNEE(S): Hoffmann-La Roche, F., und Co. A.-G., Switz.
SOURCE: Jpn. Kokai Tokkyo Koho, 10 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 63041474	A2	19880222	JP 1987-190527	19870731
US 4885309	A	19891205	US 1986-893076	19860801
ZA 8705064	A	19881026	ZA 1987-5064	19870710
IL 83379	A1	19911121	IL 1987-83379	19870730
DK 8704013	A	19880202	DK 1987-4013	19870731
EP 262334	A2	19880406	EP 1987-111134	19870731
EP 262334	A3	19900131		
R: BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
HU 46534	A2	19881128	HU 1987-3526	19870731
HU 203470	B	19910828		
CA 1303507	A1	19920616	CA 1987-543535	19870731
AU 8776566	A1	19880204	AU 1987-76566	19870803

AU 601458 B2 19900913
PRIORITY APPLN. INFO.: US 1986-893076 19860801
OTHER SOURCE(S): MARPAT 110:33733
IT **96566-25-5**
RL: BIOL (Biological study)
(antiinflammatory agent contg.)
RN 96566-25-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 6-acetyl-7-[[5-(4-acetyl-3-hydroxy-2-propylphenoxy)pentyl]oxy]-3,4-dihydro- (9CI) (CA INDEX NAME)



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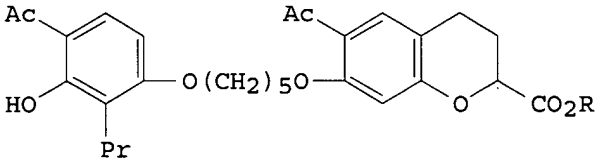


I

AB Antiinflammatory agents are comprised of benzopyran derivs. I (R = H, alkyl). (.+-.)-I (R = H) showed (68 .+-. 7)% inhibition of arachidonic acid-induced ear edema in mice at 2.0 mg in topical application. An ointment was formulated from 1 g (.+-.)-I (R = H) and 100 g white vaseline.

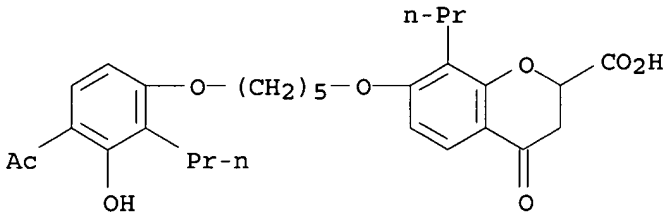
L3 ANSWER 98 OF 101 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1986:5775 CAPLUS
DOCUMENT NUMBER: 104:5775
TITLE: Substituted dihydrobenzopyran-2-carboxylates
INVENTOR(S): Miyano, Masateru; Shone, Robert Larry
PATENT ASSIGNEE(S): Searle, G. D., and Co., USA
SOURCE: Eur. Pat. Appl., 48 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 150447	A2	19850807	EP 1984-115838	19841219
EP 150447	A3	19860528		
EP 150447	B1	19900124		
R: DE, FR, GB, IT				
US 4565882	A	19860121	US 1984-568846	19840106
JP 60158187	A2	19850819	JP 1985-74	19850104
JP 06031206	B4	19940427		

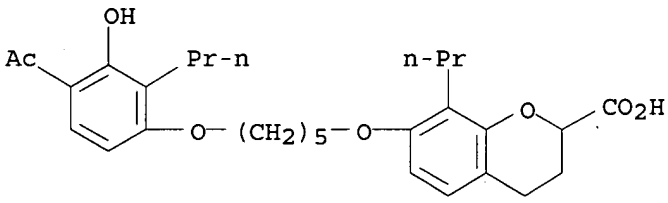
PRIORITY APPLN. INFO.: US 1984-568846 19840106
OTHER SOURCE(S): CASREACT 104:5775
IT **99453-88-0P 99453-91-5P 99453-93-7P**
99453-97-1P 99453-98-2P 99453-99-3P

99454-04-3P 99454-06-5P 99454-10-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as allergy inhibitor and antiinflammatory)

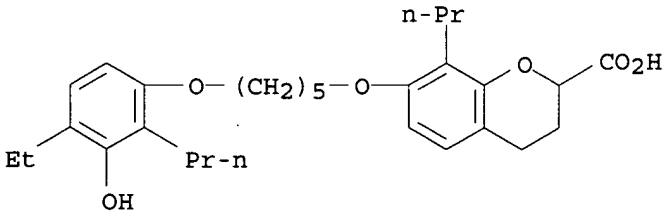
RN 99453-88-0 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[[5-(4-acetyl-3-hydroxy-2-propylphenoxy)pentyl]oxy]-3,4-dihydro-4-oxo-8-propyl- (9CI) (CA INDEX NAME)



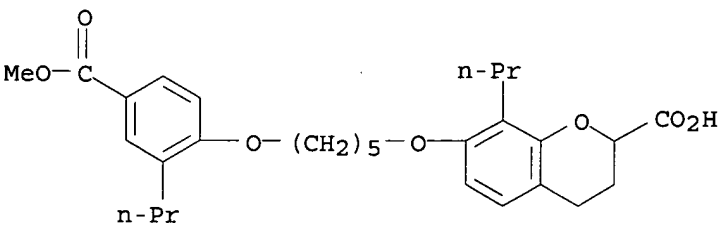
RN 99453-91-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[[5-(4-acetyl-3-hydroxy-2-propylphenoxy)pentyl]oxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



RN 99453-93-7 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[[5-(4-ethyl-3-hydroxy-2-propylphenoxy)pentyl]oxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)

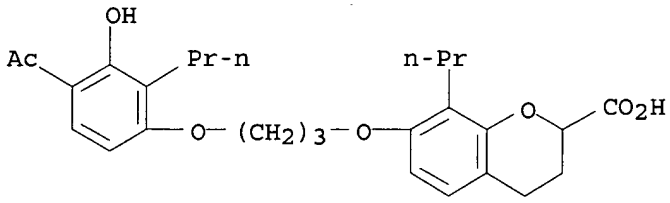


RN 99453-97-1 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 3,4-dihydro-7-[[5-[4-(methoxycarbonyl)-2-propylphenoxy]pentyl]oxy]-8-propyl- (9CI) (CA INDEX NAME)

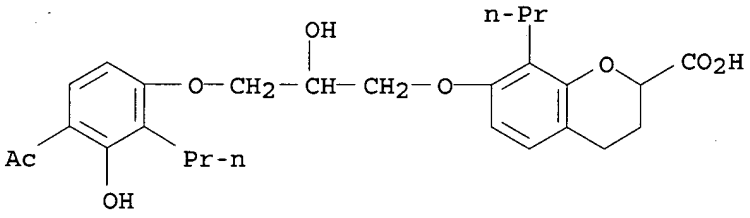


RN 99453-98-2 CAPLUS

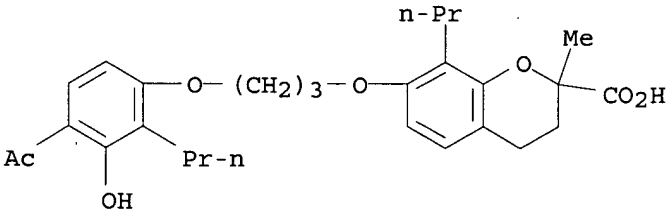
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-3-hydroxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



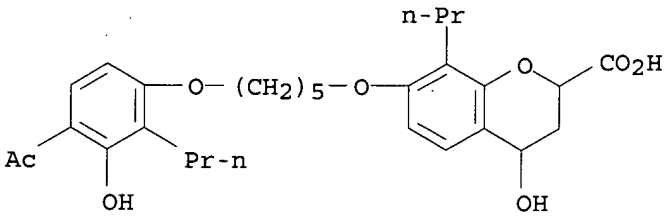
RN 99453-99-3 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-3-hydroxy-2-propylphenoxy)-2-hydroxypropoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



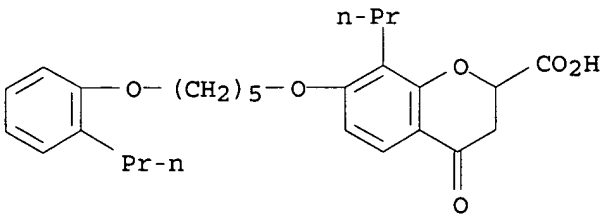
RN 99454-04-3 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-3-hydroxy-2-propylphenoxy)propoxy]-3,4-dihydro-2-methyl-8-propyl- (9CI) (CA INDEX NAME)



RN 99454-06-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[[5-(4-acetyl-3-hydroxy-2-propylphenoxy)pentyl]oxy]-3,4-dihydro-4-hydroxy-8-propyl- (9CI) (CA INDEX NAME)



RN 99454-10-1 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 3,4-dihydro-4-oxo-8-propyl-7-[[5-(2-propylphenoxy)pentyl]oxy]- (9CI) (CA INDEX NAME)



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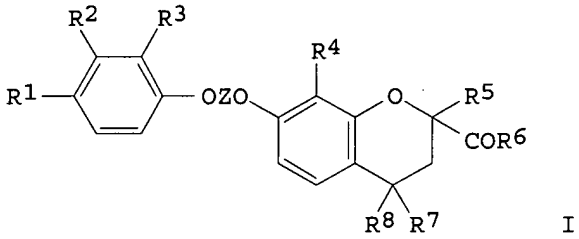
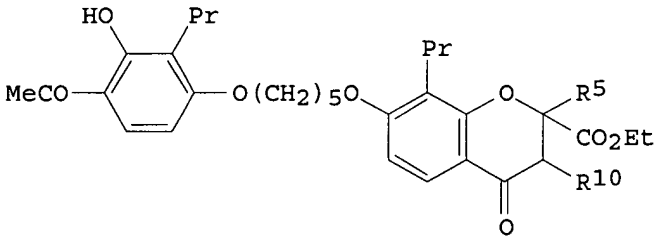


I



II

AB Antiallergy and antiinflammatory (no data) title compds. I (R1 = H, Et, MeCO, MeCHOH, EtO2C; R2 = H, OH, alkanoyloxy, CH2:CHCH2CH2CO2; R3, R4 = H, alkyl, CH2:CHCH2; R5 = H, alkanoyl; R6 = H, R9O; R7 = H, R8 = H, OH, alkoxy, CH2:CHCH2CH2O; R7R8 = O; R9 = H, alkyl, alkali metal, ammonium; Z = (hydroxy)alkylene] were prepd. Thus, 3,2,4-Pr(HO)2C6H2COMe was alkylated with Br(CH2)5Br to give 73% 2,3,4-Pr(HO)(MeCO)C6H2O(CH2)5Br. This was condensed with Et 7-hydroxy-8-propyl-4-oxo-4H-1-benzopyran-2-carboxylate to give 44% (pentyloxy)chromone II (R5R10 = bond) which was hydrogenated over Raney Ni to give 51% II (R5, R10 = H).

L3 ANSWER 99 OF 101 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1985:560389 CAPLUS
DOCUMENT NUMBER: 103:160389
TITLE: Benzopyran antimetabolites
PATENT ASSIGNEE(S): Searle, G. D., and Co., USA
SOURCE: Jpn. Kokai Tokkyo Koho, 31 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 60042378	A2	19850306	JP 1984-14978	19840130
JP 62008432	B4	19870223		

AU 8423157	A1	19850214	AU 1984-23157	19840109
AU 548450	B2	19851212		
ZA 8400345	A	19850227	ZA 1984-345	19840117
EP 139809	A1	19850508	EP 1984-100466	19840118
EP 139809	B1	19880727		
R: BE, CH, DE, FR, GB, IT, LI, NL, SE				
EP 254329	A1	19880127	EP 1987-112296	19840118
EP 254329	B1	19900926		
R: BE, CH, DE, FR, GB, IT, LI, NL, SE				
CA 1270834	A1	19900626	CA 1984-446171	19840127
US 4778903	A	19881018	US 1984-681038	19841212
US 4665203	A	19870512	US 1985-764697	19850812
JP 62070368	A2	19870331	JP 1986-186103	19860807
JP 02050113	B4	19901101		
US 4952705	A	19900828	US 1987-13807	19870212
US 4888356	A	19891219	US 1988-206624	19880614

PRIORITY APPLN. INFO.:

US 1983-520973	19830808
US 1983-560355	19831212
EP 1984-100466	19840118
US 1984-681038	19841212
US 1985-764697	19850812

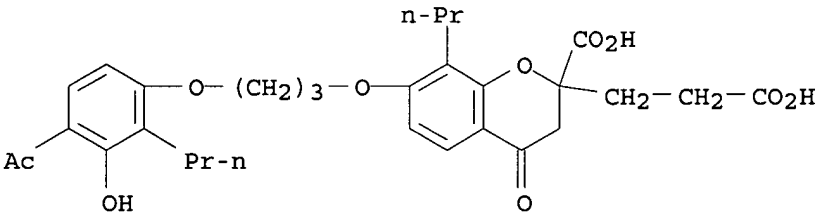
OTHER SOURCE(S): CASREACT 103:160389

IT **98193-16-9P 98193-69-2P**

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

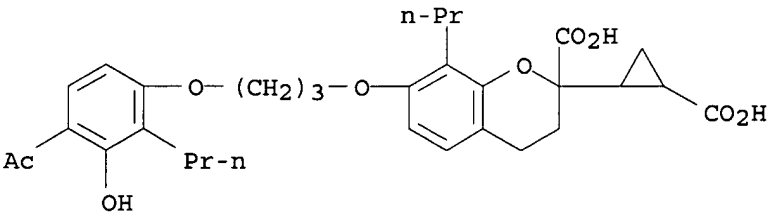
RN 98193-16-9 CAPLUS

CN 2H-1-Benzopyran-2-propanoic acid, 7-[3-(4-acetyl-3-hydroxy-2-propylphenoxy)propoxy]-2-carboxy-3,4-dihydro-4-oxo-8-propyl- (9CI) (CA INDEX NAME)

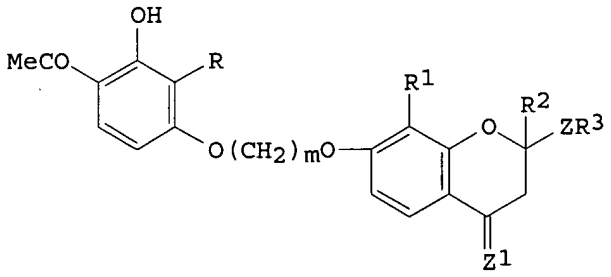


RN 98193-69-2 CAPLUS

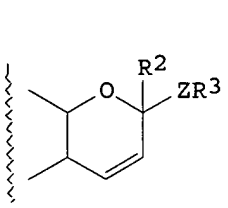
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-3-hydroxy-2-propylphenoxy)propoxy]-2-(2-carboxycyclopropyl)-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



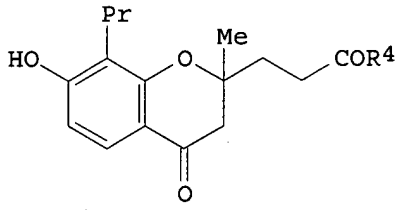
GI



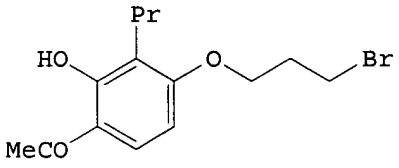
I



II



III



V

AB Benzopyrans I and II (R, R1 = alkyl; R2 = alkyl, carboxyl, alkoxycarbonylalkyl; R3 = H, carboxyl, alkoxycarbonyl, aminocarbonyl, OH; Z = alkylene, alkenylene, etc.; Z1 = O; H2; H, OH; m = 2-6), useful as leukotriene D4 inhibitors, were prepd. Thus, refluxing 2,4-dihydroxy-3-propylacetophenone with Et levulinate and pyrrolidine in PhMe gave benzopyranes III [R4 = EtO (IV), pyrrolidino]. Stirring IV with bromide V and K2CO3 in DMF gave I (R = R1 = Pr, R2 = Me, R3 = EtO, Z = CH2CH2, Z1 = O, m = 3).

L3 ANSWER 100 OF 101 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1985:406223 CAPLUS
DOCUMENT NUMBER: 103:6223
TITLE: Phenoxyalkoxy-3,4-dihydro-2H-1-benzopyran derivatives
INVENTOR(S): Cohen, Noal; Weber, Giuseppe F.
PATENT ASSIGNEE(S): Hoffmann-La Roche, F., und Co. A.-G., Switz.
SOURCE: Eur. Pat. Appl., 109 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 129906	A1	19850102	EP 1984-107289	19840625
EP 129906	B1	19880608		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
US 4785017	A	19881115	US 1984-614368	19840529
ZA 8404519	A	19850227	ZA 1984-4519	19840614
FI 8402497	A	19841225	FI 1984-2497	19840620
FI 87207	B	19920831		
FI 87207	C	19921210		
DK 8403047	A	19841225	DK 1984-3047	19840621
IL 72187	A1	19900209	IL 1984-72187	19840621
NO 8402549	A	19841227	NO 1984-2549	19840622
NO 168643	B	19911209		

NO 168643	C	19920318			
AU 8429785	A1	19850103	AU 1984-29785	19840622	
AU 565490	B2	19870917			
BR 8403068	A	19850528	BR 1984-3068	19840622	
HU 36816	A2	19851028	HU 1984-2427	19840622	
HU 202512	B	19910328			
CS 246085	B2	19861016	CS 1984-4772	19840622	
JP 60019782	A2	19850131	JP 1984-128475	19840623	
JP 04069153	B4	19921105			
ES 533678	A1	19851001	ES 1984-533678	19840623	
AT 34981	E	19880615	AT 1984-107289	19840625	
ES 541709	A1	19851201	ES 1985-541709	19850329	
CS 246098	B2	19861016	CS 1985-3161	19850430	
US 4788214	A	19881129	US 1986-907244	19860915	
ZA 8607083	A	19880427	ZA 1986-7083	19860917	
CA 1281030	A1	19910305	CA 1986-518504	19860918	
AU 590798	B2	19891116	AU 1986-63013	19860922	
AU 8663013	A1	19880324			

PRIORITY APPLN. INFO.:

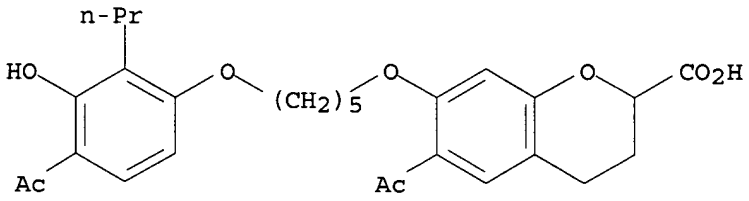
US 1983-507383 19830624
US 1984-614368 19840529
CS 1984-4772 19840622
EP 1984-107289 19840625
US 1985-758256 19850724

OTHER SOURCE(S): CASREACT 103:6223

IT **96565-55-8P 96566-19-7P 96566-22-2P**
96566-24-4P 96566-26-6P 96566-28-8P
96566-45-9P 96566-51-7P 96566-60-8P
96566-63-1P 96566-64-2P 96566-65-3P
96566-66-4P 96566-67-5P 96566-68-6P
96566-69-7P 96594-21-7P 96686-71-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and antiallergy activity of)

RN 96565-55-8 CAPLUS

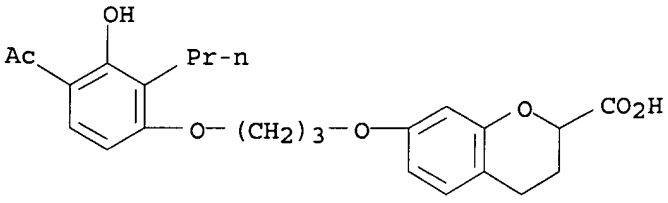
CN 2H-1-Benzopyran-2-carboxylic acid, 6-acetyl-7-[[5-(4-acetyl-3-hydroxy-2-propylphenoxy)pentyl]oxy]-3,4-dihydro-, monosodium salt (9CI) (CA INDEX NAME)



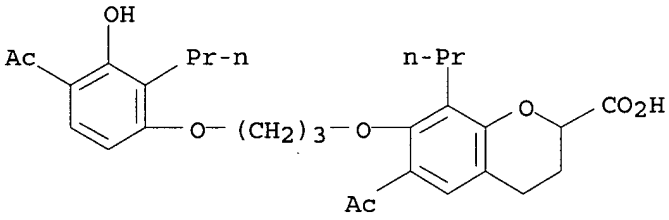
● Na

RN 96566-19-7 CAPLUS

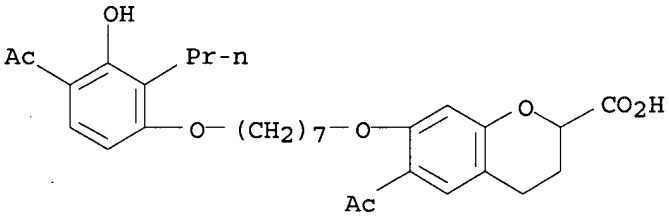
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-3-hydroxy-2-propylphenoxy)propoxy]-3,4-dihydro- (9CI) (CA INDEX NAME)



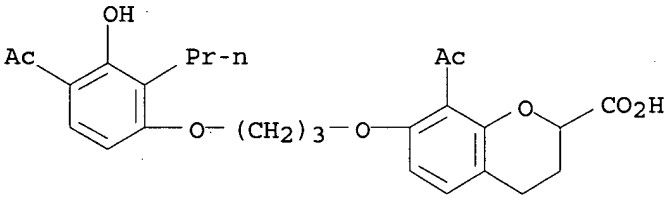
RN 96566-22-2 CAPLUS
RN 96566-24-4 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 6-acetyl-7-[3-(4-acetyl-3-hydroxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



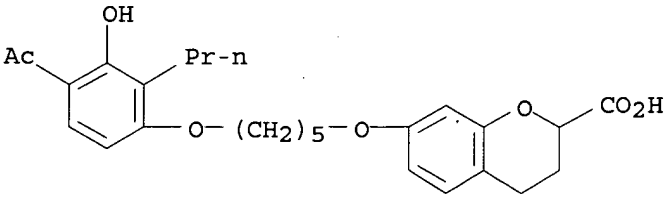
RN 96566-26-6 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 6-acetyl-7-[[7-(4-acetyl-3-hydroxy-2-propylphenoxy)heptyl]oxy]-3,4-dihydro- (9CI) (CA INDEX NAME)



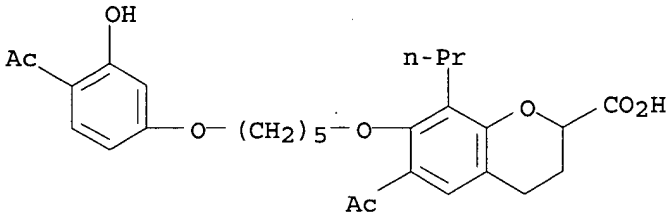
RN 96566-28-8 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 8-acetyl-7-[3-(4-acetyl-3-hydroxy-2-propylphenoxy)propoxy]-3,4-dihydro- (9CI) (CA INDEX NAME)



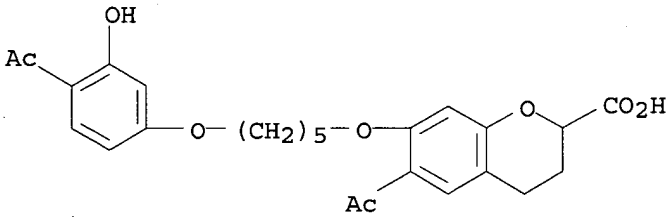
RN 96566-45-9 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[[5-(4-acetyl-3-hydroxy-2-propylphenoxy)pentyl]oxy]-3,4-dihydro- (9CI) (CA INDEX NAME)



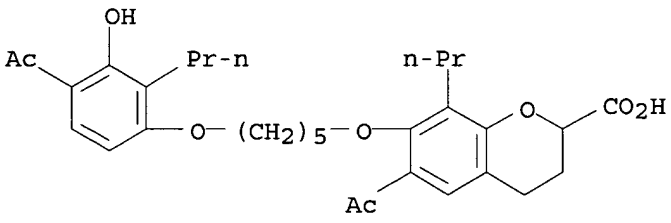
RN 96566-51-7 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 6-acetyl-7-[[5-(4-acetyl-3-hydroxyphenoxy)pentyl]oxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



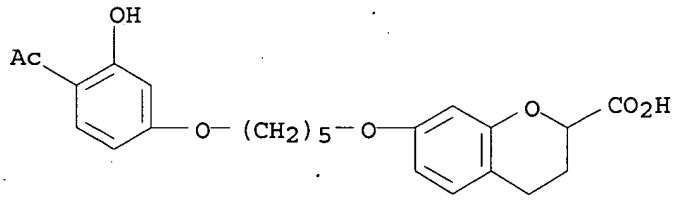
RN 96566-60-8 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 6-acetyl-7-[[5-(4-acetyl-3-hydroxyphenoxy)pentyl]oxy]-3,4-dihydro- (9CI) (CA INDEX NAME)



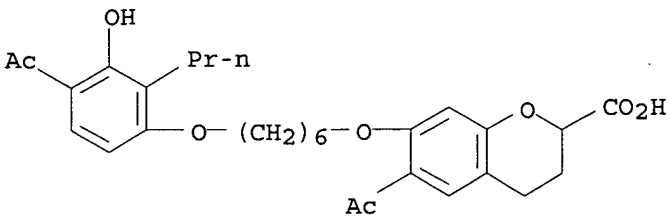
RN 96566-63-1 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 6-acetyl-7-[[5-(4-acetyl-3-hydroxy-2-propylphenoxy)pentyl]oxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



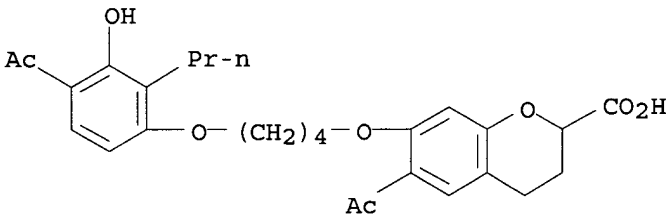
RN 96566-64-2 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[[5-(4-acetyl-3-hydroxyphenoxy)pentyl]oxy]-3,4-dihydro- (9CI) (CA INDEX NAME)



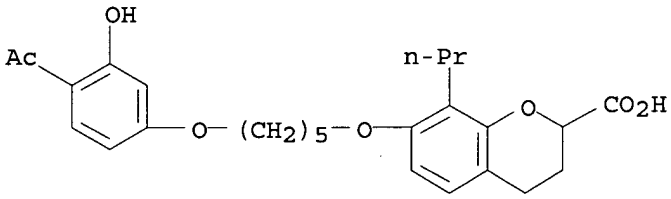
RN 96566-65-3 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 6-acetyl-7-[[6-(4-acetyl-3-hydroxy-2-propylphenoxy)hexyl]oxy]-3,4-dihydro- (9CI) (CA INDEX NAME)



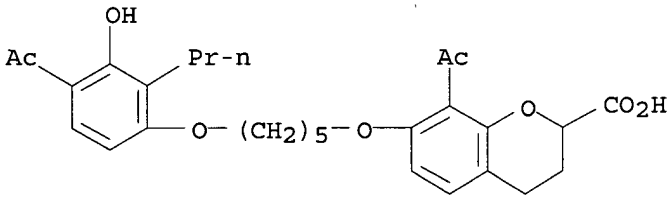
RN 96566-66-4 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 6-acetyl-7-[4-(4-acetyl-3-hydroxy-2-propylphenoxy)butoxy]-3,4-dihydro- (9CI) (CA INDEX NAME)



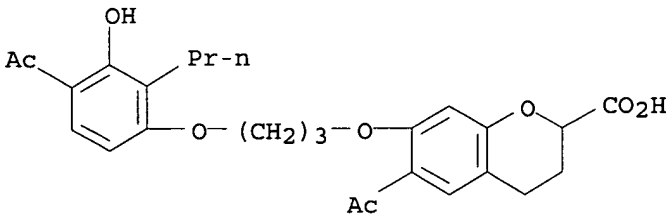
RN 96566-67-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[[5-(4-acetyl-3-hydroxyphenoxy)pentyl]oxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



RN 96566-68-6 CAPLUS
RN 96566-69-7 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 8-acetyl-7-[[5-(4-acetyl-3-hydroxy-2-propylphenoxy)pentyl]oxy]-3,4-dihydro- (9CI) (CA INDEX NAME)

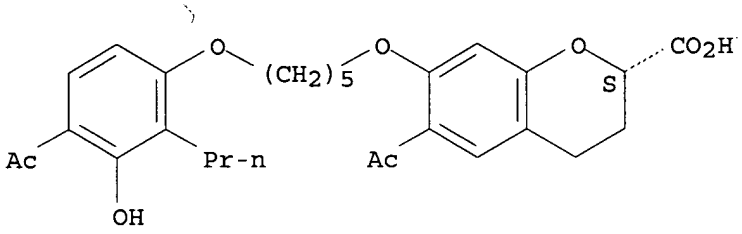


RN 96594-21-7 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 6-acetyl-7-[3-(4-acetyl-3-hydroxy-2-propylphenoxy)propoxy]-3,4-dihydro- (9CI) (CA INDEX NAME)



RN 96686-71-4 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 6-acetyl-7-[[5-(4-acetyl-3-hydroxy-2-propylphenoxy)pentyl]oxy]-3,4-dihydro-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

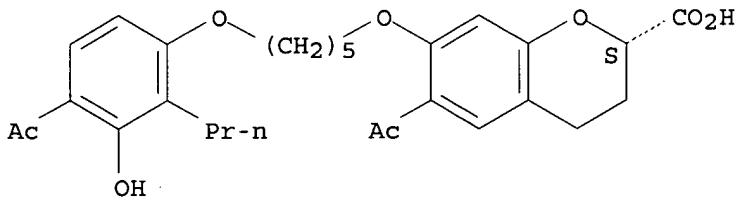


IT **96686-72-5P 96686-74-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and conversion to free acid)
RN 96686-72-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 6-acetyl-7-[[5-(4-acetyl-3-hydroxy-2-propylphenoxy)pentyl]oxy]-3,4-dihydro-, (S)-, compd. with (R)-.alpha.-methylbenzenemethanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 96686-71-4
CMF C28 H34 O8

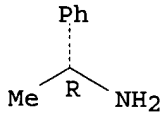
Absolute stereochemistry.



CM 2

CRN 3886-69-9
CMF C8 H11 N

Absolute stereochemistry.



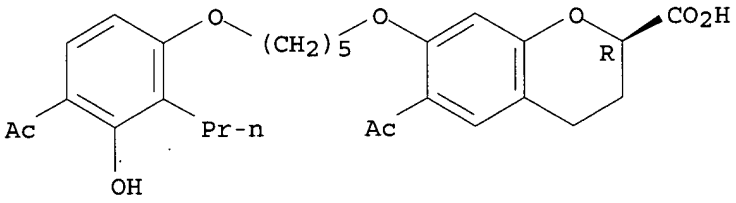
RN 96686-74-7 CAPLUS

CN 2H-1-Benzopyran-2-carboxylic acid, 6-acetyl-7-[[5-(4-acetyl-3-hydroxy-2-propylphenoxy)pentyl]oxy]-3,4-dihydro-, (R)-, compd. with (R)-.alpha.-methylbenzenemethanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 96686-73-6
CMF C28 H34 O8

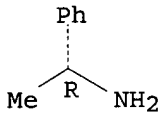
Absolute stereochemistry.



CM 2

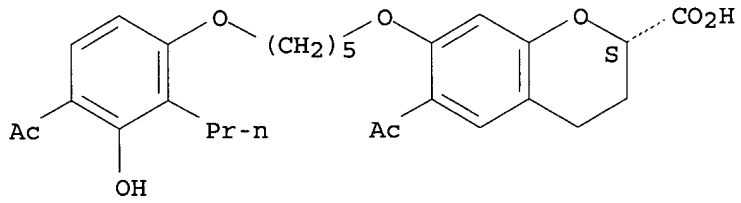
CRN 3886-69-9
CMF C8 H11 N

Absolute stereochemistry.

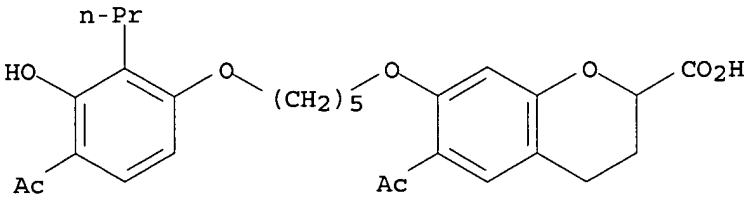


IT **96686-71-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and esterification of)
RN 96686-71-4 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 6-acetyl-7-[[5-(4-acetyl-3-hydroxy-2-propylphenoxy)pentyl]oxy]-3,4-dihydro-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

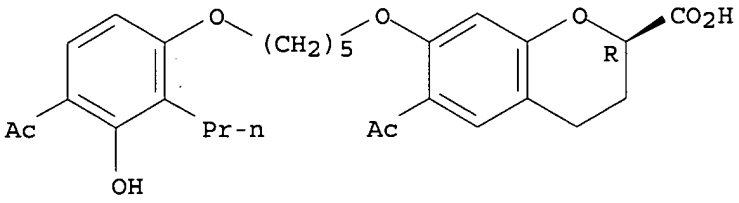


IT **96566-25-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction of, with sodium hydroxide or resoln. of)
RN 96566-25-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 6-acetyl-7-[[5-(4-acetyl-3-hydroxy-2-propylphenoxy)pentyl]oxy]-3,4-dihydro- (9CI) (CA INDEX NAME)



IT **96686-73-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn., esterification, and antiallergy activity of)
RN 96686-73-6 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 6-acetyl-7-[[5-(4-acetyl-3-hydroxy-2-propylphenoxy)pentyl]oxy]-3,4-dihydro-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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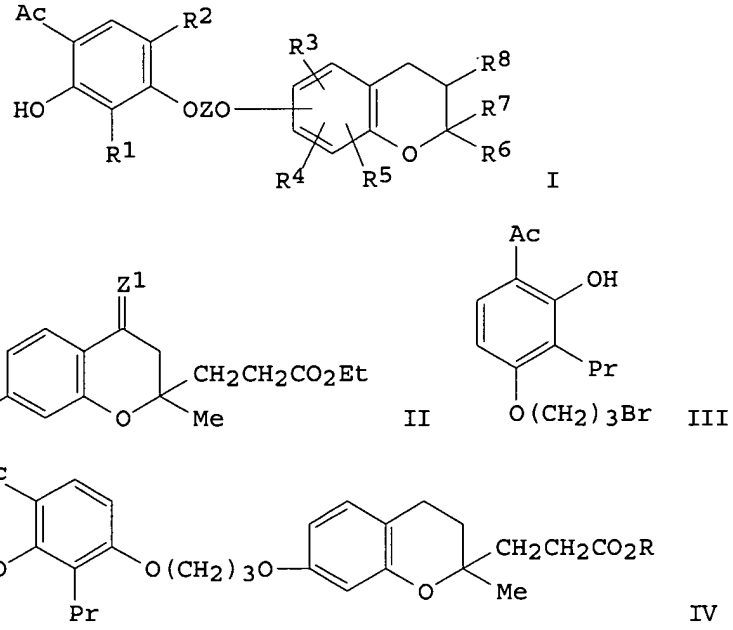


AB Benzopyran derivs. I [R1 = H, alkyl; R2 = H, halo; R3, R4 , R5 = H, acyl, alkyl; R6, R7 = H, R8 = CO2R9; R6 = H, alkyl, R7 = (CH2)nCO2R9, R8 = H; R9 = H, alkyl; Z = C3-7 alkylene; n = 0-4] and, when R9 = H, their salts with pharamceutically tolerable bases, useful in treating allergy, were prepd. Refluxing a mixt. of 2,4-(HO)2C6H3COMe, MeCOCH2CH2CO2Et, pyrrolidine, and PhMe 3 h with stirring gave 58.1% benzopyranpropanoate (.+-.)-II (Z1 = O),

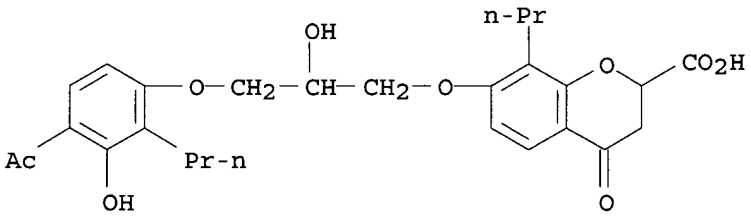
redn. of which with BF3.Et2O and BH3 in THF gave 63.1% (.+-.)-II (Z1 = H2). Treating NaH-mineral oil in DMF with (.+-.)-II (Z1 = H2) in DMF, then with acetophenone III in DMF gave 46.5% diether (.+-.)-IV (R = Et), sapon. of which in 1:1 THF-H2O with LiOH.H2O in 22 h at room temp. gave 95.8% (.+-.)-IV (R = H). (.+-.)-IV (R = H) had IC50 1 .times. 10-7 in the guinea pig ileum test of SRS-A antagonism.

L3 ANSWER 101 OF 101 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1983:575604 CAPLUS
DOCUMENT NUMBER: 99:175604
TITLE: Anti-SRS-A carboxylic acid derivatives and pharmaceutical formulations containing them
INVENTOR(S): Bantick, John Raymond
PATENT ASSIGNEE(S): Fisons Ltd., UK
SOURCE: Eur. Pat. Appl., 67 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

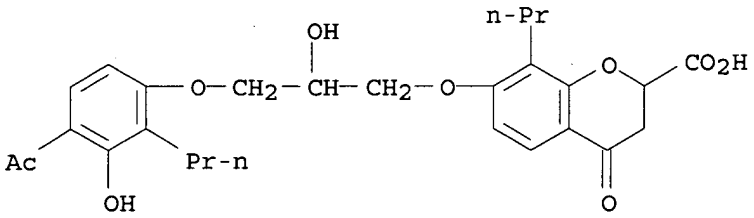
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 79637	A1	19830525	EP 1982-201368	19821101
EP 79637	B1	19870128		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
US 4474788	A	19841002	US 1982-438163	19821101
AT 25251	E	19870215	AT 1982-201368	19821101
JP 58090557	A2	19830530	JP 1982-196883	19821111

PRIORITY APPLN. INFO.: GB 1981-34186 19811112
EP 1982-201368 19821101

IT **87472-31-9P 87491-55-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 87472-31-9 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-3-hydroxy-2-propylphenoxy)-2-hydroxypropoxy]-3,4-dihydro-4-oxo-8-propyl- (9CI) (CA INDEX NAME)

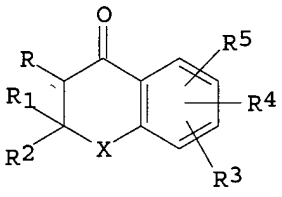


RN 87491-55-2 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-3-hydroxy-2-propylphenoxy)-2-hydroxypropoxy]-3,4-dihydro-4-oxo-8-propyl-, monosodium salt (9CI) (CA INDEX NAME)



● Na

GI



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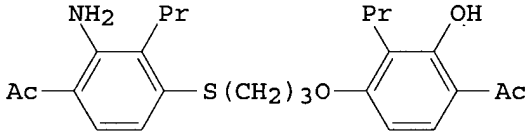

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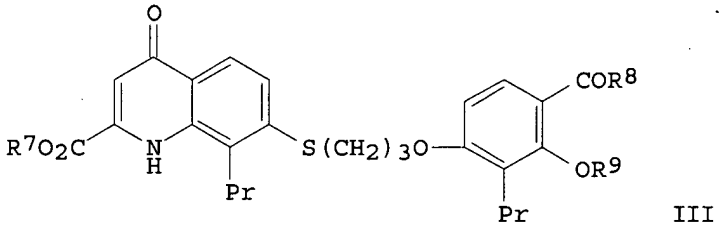

III

AB Anti-allergy (no data) bicyclic compds. I [R, R1 = H, alkyl; RR1 = bond; R2 = CO2H, carboxyalkyl; R3 = substituted OH, SH, NH2; R4, R5 = H, halogen, (un)substituted OH, NH2, alkyl, acyl; X = S, O, NR6 (R6 = H, alkyl)] were prepd. Thus, 3,2,4-Pr(HO)2C6H2Ac reacted with 4,2,3-AcPr(H2N)C6H2S(CH2)3Br to give phenol II, which cyclized with EtO2CCO2Et to give quinoline III [R7 = Et, R8R9 = CH:C(CO2Et)]. The latter compd. gave III (R7 = H, R8 = Me, R9 = H) on hydrolysis.

=> d his

(FILE 'HOME' ENTERED AT 18:15:27 ON 19 NOV 2002)

FILE 'REGISTRY' ENTERED AT 18:15:34 ON 19 NOV 2002
L1 STRUCTURE UPLOADED
L2 155 S L1 FUL

FILE 'CAPLUS' ENTERED AT 18:16:08 ON 19 NOV 2002
L3 101 S L2

=> s l3 and (disease or condition or disorder)
562857 DISEASE
152340 DISEASES
638393 DISEASE
(DISEASE OR DISEASES)
223846 CONDITION

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       1376783 CONDITIONS
       1553636 CONDITION
                 (CONDITION OR CONDITIONS)
        211660 DISORDER
        111317 DISORDERS
        293073 DISORDER
                 (DISORDER OR DISORDERS)
L4          48 L3 AND (DISEASE OR CONDITION OR DISORDER)

=> d l4 ibib hitstr abs 1-48

L4   ANSWER 1 OF 48  CAPLUS  COPYRIGHT 2002 ACS
ACCESSION NUMBER:         2002:594844  CAPLUS
DOCUMENT NUMBER:          137:140518
TITLE:                    Preparation of thiazolyl-, oxazolyl-, pyrrolyl-, and
                          imidazolyl- acid amide derivatives as inhibitors of
                          phosphodiesterase IV isozymes
INVENTOR(S):              Marfat, Anthony; McKechney, Michael William
PATENT ASSIGNEE(S):       Pfizer Products Inc., USA
SOURCE:                   PCT Int. Appl., 249 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  --------       ---------------  --------
     WO 2002060898      A1   20020808       WO 2001-IB2728   20011224
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
             CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     US 2002123520      A1   20020905       US 2002-62145    20020131
PRIORITY APPLN. INFO.:                   US 2001-265486P  P  20010131
OTHER SOURCE(S):          MARPAT 137:140518
IT   96566-25-5, Ablukast
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (combination therapy with PDE4 inhibitors; prepn. of thiazolyl-,
        oxazolyl-, pyrrolyl-, and imidazolyl- acid amide derivs. as inhibitors
        of PDE4 isoenzymes)
RN   96566-25-5  CAPLUS
CN   2H-1-Benzopyran-2-carboxylic acid, 6-acetyl-7-[[5-(4-acetyl-3-hydroxy-2-
     propylphenoxy)pentyl]oxy]-3,4-dihydro- (9CI)  (CA INDEX NAME)
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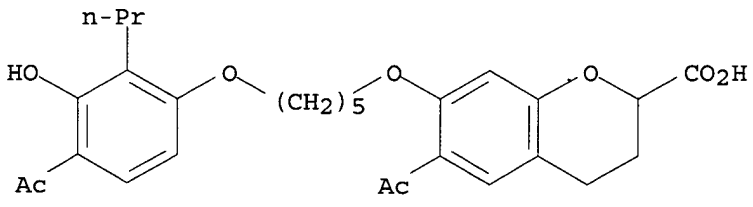

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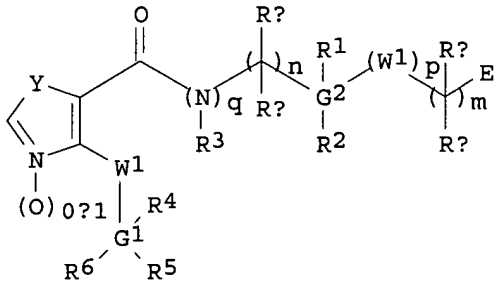

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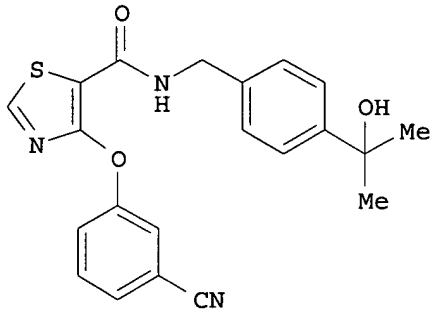


II

AB Title compds. I [wherein p = 0-1; q = 0-1; provided that when q = 0, n = 2; m = 0-3; n = 1-2; W1 and W2 = independently O, SO0-2, or NR3; or W2 = (un)substituted methylene; Y = SO0-2, O, NO0-1, NR3, or (un)substituted methylene; ; RA and RB = independently H, F, CF3, alkyl, or (un)substituted cycloalkyl, Ph, or benzyl; or when m = 1, CRARB = (un)substituted spiro; RC and RD have the same meaning as RA and RB except that one of them must be H; R1 and R2 = H, F, Cl, CN, NO2, (fluoro)alkyl, alkynyl, alkoxy, phenoxy, carbamoyl, etc.; R3 = H, alkyl, Ph, benzyl, alkoxy, phenoxy, etc.; R4, R5, and R6 = H, F, Cl, and (un)substituted (cyclo)alkyl, alkenyl, alkynyl, Ph, benzyl, pyridyl, alkoxy, phenoxy, acyl, carboxy, CN, NO2, carbamoyl, ureido, (hetero)aryl, etc.; G1 and G2 = independently (un)satd. carbocyclyl or heterocyclyl; E = (un)substituted carboxy, carbamoyl, acyl, hydroxyalkyl, cyanoalkyl, acylamino, ureido, amino, heterocyclyl, etc.] were prepd. as inhibitors of PDE4 (no data). For example, 4-(3-cyanophenoxy)thiazole-5-carboxylic acid was treated with 2-(4-aminomethylphenyl)propan-2-ol in the presence of EDCl and HOBT in DMF to give the thiazolamide II. I are useful in the treatment of **diseases** regulated by the activation and degranulation of eosinophils, esp. asthma, chronic bronchitis, and chronic obstructive pulmonary **disease** (no data). In addn., I may be used in combination therapy with a wide variety of other therapeutic agents.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 48 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:594842 CAPLUS

DOCUMENT NUMBER: 137:154859

TITLE: Preparation of carbamoyl-substituted pyridinyl aryl ether derivatives as inhibitors of phosphodiesterase IV isozymes

INVENTOR(S): Chambers, Robert James; Magee, Thomas Victor; Marfat, Anthony

PATENT ASSIGNEE(S): Pfizer Products Inc., USA

SOURCE: PCT Int. Appl., 285 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002060896	A1	20020808	WO 2001-IB2726	20011224

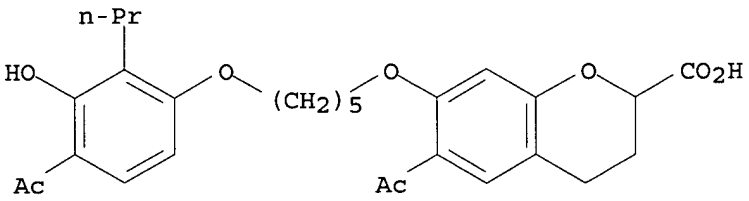
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-265304P P 20010131
OTHER SOURCE(S): MARPAT 137:154859

IT **96566-25-5**, Ablukast
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapy with PDE4 inhibitors; prepn. of carbamoyl-substituted pyridinyl aryl ether derivs. as inhibitors of PDE4 isoenzymes)

RN 96566-25-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 6-acetyl-7-[[5-(4-acetyl-3-hydroxy-2-propylphenoxy)pentyl]oxy]-3,4-dihydro- (9CI) (CA INDEX NAME)



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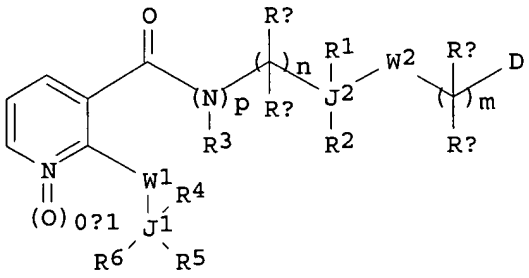

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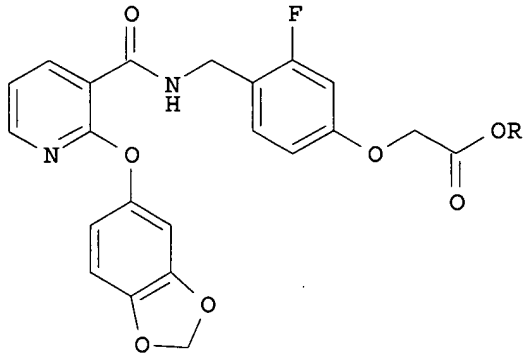


II

AB Title compds. compds. I [wherein p = 0-1, provided that when p = 0, n = 2; m = 1-3; n = 1-2; W1 and W2 = independently O, S(O)0-2, or NR3; Y = =C(R1a) or N(O)0-1; R1a = H, F, Cl, CN, NO2, (fluoro)alkyl, alkynyl, fluoroalkoxy, OR16, or (un)substituted carbamoyl; RA and RB = independently H, F, CF3, or (un)substituted (cyclo)alkyl, Ph, or benzyl; or CRARB = spiro moiety; RC and RD = the same as RA and RB except that one of them must be H; R1 and R2 = independently H, F, Cl, CN, NO2, (fluoro)alkyl, alkynyl, OR16, or (un)substituted carbamoyl; R3 = H, alkyl, Ph, benzyl, or OR16; R4, R5 and R6 = independently H, F. Cl, alkynyl, R16, OR16, SO0-2R16, COR16, CO2R16, OCOR16, CN, NO2, (un)substituted carbamoyl(oxy), ureido, carboximidoyl, aryl, heterocyclyl, etc.; or R5 and R6 taken together with the atoms to which they are attached = (hetero)cyclyl; J1 and J2 = independently (un)substituted, (un)satd. monocyclic or fused polycyclic ring; D = (un)substituted carboxy, carbamoyl, acyl, hydroxy(alkyl), cyano(alkyl), etc.; R16 = H or (un)substituted (cyclo)alkyl, alkenyl, Ph, benzyl, or pyridyl] were prepd. as inhibitors of PDE4 (no data). For example, 2-(benzo[1,3]dioxol-5-yloxy)nicotinic acid was coupled with (4-aminomethyl-3-fluorophenoxy)acetic acid Me ester in the presence of 1-hydroxybenzotriazole.bul.H2O and 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide.bul.HCl in DMF/CH2Cl2 to give the pyridinecarboxamide II (R = Me) in 38% yield. Sapon. using aq. LiOH in THF and MeOH afforded the desired acid II (R = OH) in 21% yield. I are useful in the treatment of **diseases** regulated by the activation and degranulation of eosinophils, esp. asthma, chronic bronchitis, and chronic obstructive pulmonary **disease** (no data). In addn., I may be used in combination therapy with a wide variety of other therapeutic agents.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 48 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:594822 CAPLUS

DOCUMENT NUMBER: 137:154857

TITLE: Preparation of nicotinamide biaryl derivatives as inhibitors of PDE4 isozymes

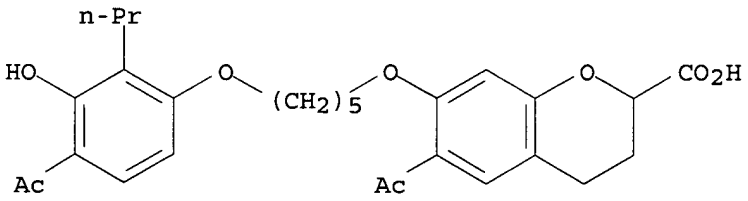
INVENTOR(S): Chambers, Robert James; Magee, Thomas Victor; Marfat,

Anthony
PATENT ASSIGNEE(S): Pfizer Productors Inc., USA
SOURCE: PCT Int. Appl., 224 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002060875	A1	20020808	WO 2001-IB2341	20011206

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-265492P P 20010131
OTHER SOURCE(S): MARPAT 137:154857
IT **96566-25-5**, Ablukast
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in combination with; prepn. of biaryl nicotinamides as inhibitors of PDE4 isoenzymes)
RN 96566-25-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 6-acetyl-7-[[5-(4-acetyl-3-hydroxy-2-propylphenoxy)pentyl]oxy]-3,4-dihydro- (9CI) (CA INDEX NAME)



GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I; g = 0-1; j = 0-1; provided that when j = 0, n must be 2; k = 0-1; m = 0-2; n = 1-2; W1 = 0, SOt (t = 0-2), NR3; W2 = OCR9R10, or absent; Y = CR1, NOk (k = 0-1); R9, R10 = H, F, CF3, etc.; or R9 and R10 are taken together, but only in the case where m = 1, to form a spiro moiety; R7, R8 have the same meaning as R9, R10 except that one of them must be H; R1, R2 = H, F, Cl, etc.; R3 = H, alkyl, Ph, etc.; R4-R6 = H, F, Cl, etc.; Q1 = Ph, benzodioxyl, etc.; Q2 = biaryl moiety], useful as inhibitors of PDE4 in the treatment of **diseases** regulated by the activation and degranulation of eosinophils, esp. asthma, chronic bronchitis, and chronic obstructive pulmonary **disease**, were prepd. E.g., a multi-step synthesis of the amide II, starting from Me 3-bromobenzoate and 4-formylbenzeneboronic acid, was given. Compds. I showed anti-inflammatory activity at 0.0001 .mu.M to 20.0 .mu.M in whole blood assay for LTE4.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 48 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:575765 CAPLUS
DOCUMENT NUMBER: 137:140435
TITLE: Benzopyrancarboxylic acid derivatives with PPAR agonist activity for the treatment of diabetes and lipid **disorders**, and their preparation, pharmaceutical compositions, and use
INVENTOR(S): Sahoo, Soumya P.; Koyama, Hiroo; Miller, Daniel J.; Boueres, Julia K.; Desai, Ranjit C.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 42 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

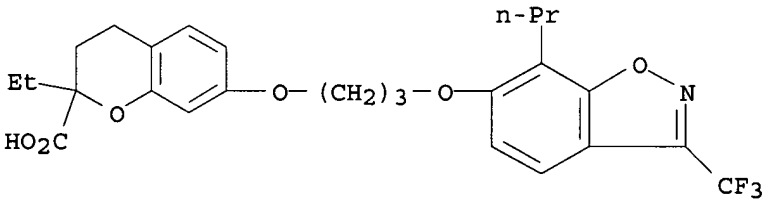
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002103242	A1	20020801	US 2001-21667	20011029
WO 2002060434	A2	20020808	WO 2001-US49501	20011026

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

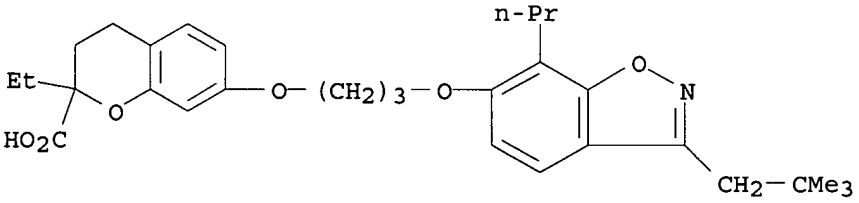
PRIORITY APPLN. INFO.: US 2000-244698P P 20001031
OTHER SOURCE(S): MARPAT 137:140435
IT **444341-48-4P**, 7-[3-(3-Trifluoromethyl-7-propylbenz[4,5]isoxazol-6-yloxy)propoxy]-2-ethylchromane-2-carboxylic acid **444341-49-5P**, 7-[3-[[3-(2,2-Dimethylpropyl)-7-propylbenz[4,5]isoxazol-6-yl]oxy]propoxy]-2-ethylchromane-2-carboxylic acid **444341-50-8P**, 7-[3-(3-Phenyl-7-propylbenz[4,5]isoxazol-6-yloxy)propoxy]-2-methylchromane-2-carboxylic acid **444341-51-9P**, 7-[3-[4-(1,2-Benzisoxazol-3-yl)-2-propylphenoxy]propoxy]-2-ethylchromane-2-carboxylic acid **444341-52-0P**, 7-[3-[2-Chloro-4-(2,2,2-trifluoroethoxy)phenoxy]propoxy]chromane-2-carboxylic acid **444341-53-1P**, 7-[3-[2-Chloro-4-(2,2,2-trifluoroethoxy)phenoxy]propoxy]-2-methylchromane-2-carboxylic acid **444341-54-2P**, 7-[3-[2-Chloro-4-(2,2,2-trifluoroethoxy)phenoxy]propoxy]-2-ethylchromane-2-carboxylic acid **444341-55-3P**, 7-[3-[2-Chloro-4-(2,2,2-trifluoroethoxy)phenoxy]propoxy]-2-propylchromane-2-carboxylic acid **444341-56-4P**, 7-[3-[2-Propyl-4-(2,2,2-trifluoroethoxy)phenoxy]propoxy]-2-ethylchromane-2-carboxylic acid **444341-57-5P**, 7-[3-(2-Chloro-4-tert-butylphenoxy)propoxy]-2-methylchromane-2-carboxylic acid **444341-58-6P**, 7-[3-(2-Chloro-4-cyclohexylphenoxy)propoxy]-2-methylchromane-2-carboxylic acid **444341-59-7P**, 7-[3-(2-Chloro-4-cyclohexylphenoxy)propoxy]-2-ethylchromane-2-carboxylic acid **444341-60-0P**, (2R)-7-[3-[2-Chloro-4-(4-tetrahydropyranyl)phenoxy]propoxy]-2-ethylchromane-2-carboxylic acid **444341-62-2P**, (2R)-7-[3-[2-Chloro-4-(4,4-dimethylcyclohexyl)phenoxy]propoxy]-2-ethylchromane-2-carboxylic acid **444341-63-3P**, (2R)-7-[3-(2-Chloro-4-cyclohexylphenoxy)propoxy]-2-ethylchromane-2-carboxylic acid **444341-64-4P**, (2R)-7-[3-(2-Chloro-4-isopropylphenoxy)propoxy]-2-ethylchromane-2-carboxylic acid **444341-65-5P**, (2R)-7-[3-(2-Chloro-4-tert-butylphenoxy)propoxy]-2-ethylchromane-2-carboxylic acid **444341-66-6P**,

(2R)-7-[3-(2-Chloro-4-isobutylphenoxy)propoxy]-2-ethylchromane-2-carboxylic acid **444341-67-7P**, (2R)-7-[3-(2-Chloro-4-trifluoromethylphenoxy)propoxy]-2-ethylchromane-2-carboxylic acid **444341-68-8P**, (2R)-7-[3-(2-Chloro-4-trifluoromethoxyphenoxy)propoxy]-2-ethylchromane-2-carboxylic acid **444341-69-9P**, (2R)-7-[3-[2-Chloro-4-(2,2,2-trifluoroethoxy)phenoxy]propoxy]-2-ethylchromane-2-carboxylic acid **444341-70-2P**, (2S)-7-[3-[2-Chloro-4-(2,2,2-trifluoroethoxy)phenoxy]propoxy]-2-ethylchromane-2-carboxylic acid **444341-71-3P**, (2R)-7-[3-(2-Chloro-4-cyclohexylphenoxy)propoxy]-2-methylchromane-2-carboxylic acid **444341-72-4P**, (2R)-7-[3-(2-Chloro-4-cyclopentylphenoxy)propoxy]-2-methylchromane-2-carboxylic acid **444341-73-5P**, (2R)-7-[3-(2-Chloro-4-tert-butylphenoxy)propoxy]-2-methylchromane-2-carboxylic acid **444341-74-6P**, (2R)-7-[3-(2-Chloro-4-isobutylphenoxy)propoxy]-2-methylchromane-2-carboxylic acid **444341-75-7P**, (2R)-7-[3-[2-Chloro-4-(2,2,2-trifluoroethoxy)phenoxy]propoxy]-2-methylchromane-2-carboxylic acid **444341-76-8P**, (2R)-7-[3-[2-Chloro-4-(4-tetrahydropyranyl)phenoxy]propoxy]-2-methylchromane-2-carboxylic acid **444341-77-9P**, (2S)-7-[3-[2-Chloro-4-(2,2,2-trifluoroethoxy)phenoxy]propoxy]-2-methylchromane-2-carboxylic acid
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; prepn. of benzopyrancarboxylic acid derivs. as PPAR agonists for treatment of diabetes and lipid **disorders**)

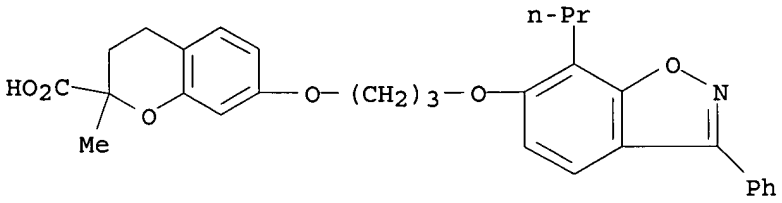
RN 444341-48-4 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 2-ethyl-3,4-dihydro-7-[3-[[7-propyl-3-(trifluoromethyl)-1,2-benzisoxazol-6-yl]oxy]propoxy]- (9CI) (CA INDEX NAME)



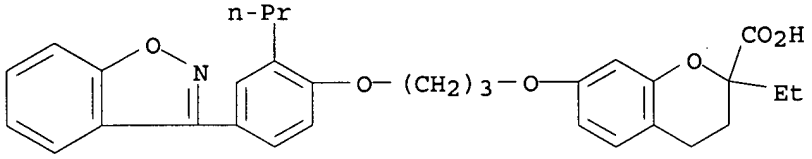
RN 444341-49-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[[3-(2,2-dimethylpropyl)-7-propyl-1,2-benzisoxazol-6-yl]oxy]propoxy]-2-ethyl-3,4-dihydro- (9CI) (CA INDEX NAME)



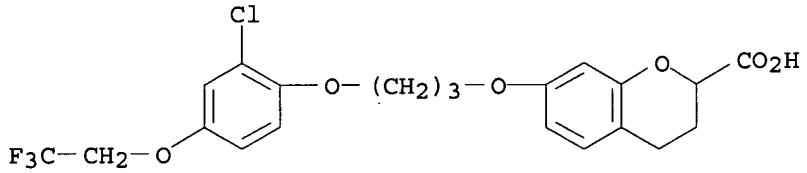
RN 444341-50-8 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 3,4-dihydro-2-methyl-7-[3-[(3-phenyl-7-propyl-1,2-benzisoxazol-6-yl)oxy]propoxy]- (9CI) (CA INDEX NAME)



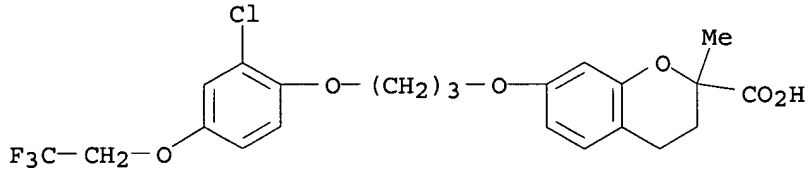
RN 444341-51-9 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[4-(1,2-benzisoxazol-3-yl)-2-propylphenoxy]propoxy]-2-ethyl-3,4-dihydro- (9CI) (CA INDEX NAME)



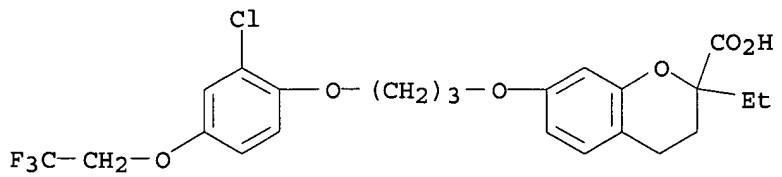
RN 444341-52-0 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[2-chloro-4-(2,2,2-trifluoroethoxy)phenoxy]propoxy]-3,4-dihydro- (9CI) (CA INDEX NAME)



RN 444341-53-1 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[2-chloro-4-(2,2,2-trifluoroethoxy)phenoxy]propoxy]-3,4-dihydro-2-methyl- (9CI) (CA INDEX NAME)

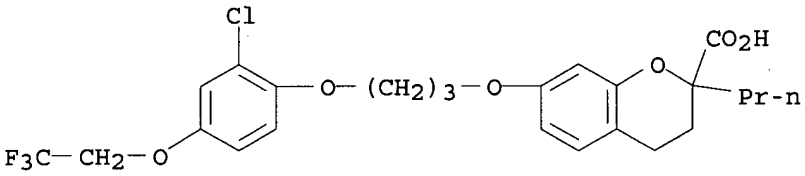


RN 444341-54-2 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[2-chloro-4-(2,2,2-trifluoroethoxy)phenoxy]propoxy]-2-ethyl-3,4-dihydro- (9CI) (CA INDEX NAME)

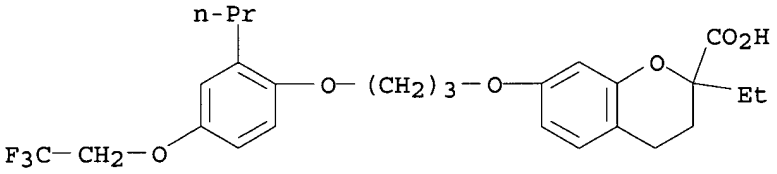


RN 444341-55-3 CAPLUS

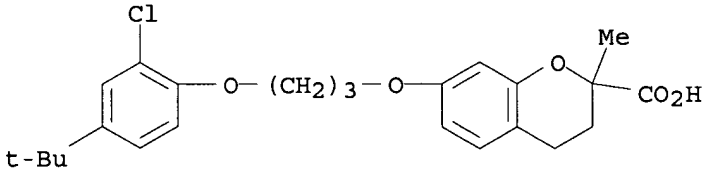
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[2-chloro-4-(2,2,2-trifluoroethoxy)phenoxy]propoxy]-3,4-dihydro-2-propyl- (9CI) (CA INDEX NAME)



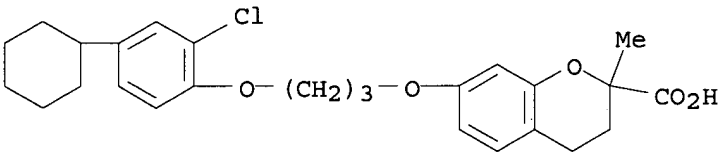
RN 444341-56-4 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 2-ethyl-3,4-dihydro-7-[3-[2-propyl-4-(2,2,2-trifluoroethoxy)phenoxy]propoxy]- (9CI) (CA INDEX NAME)



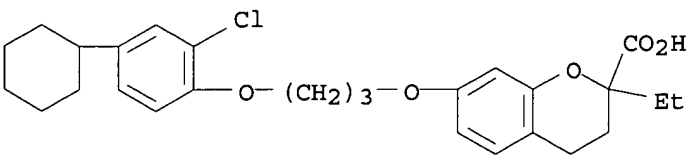
RN 444341-57-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[2-chloro-4-(1,1-dimethylethyl)phenoxy]propoxy]-3,4-dihydro-2-methyl- (9CI) (CA INDEX NAME)

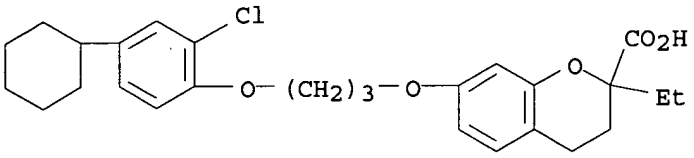


RN 444341-58-6 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(2-chloro-4-cyclohexylphenoxy)propoxy]-3,4-dihydro-2-methyl- (9CI) (CA INDEX NAME)



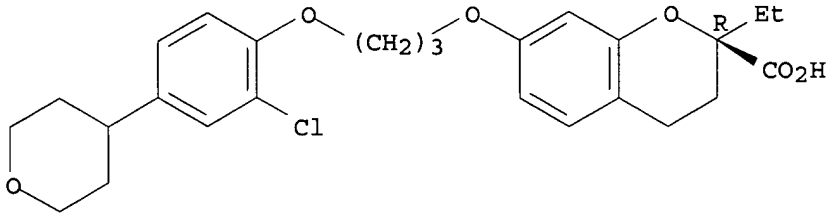
RN 444341-59-7 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(2-chloro-4-cyclohexylphenoxy)propoxy]-2-ethyl-3,4-dihydro- (9CI) (CA INDEX NAME)





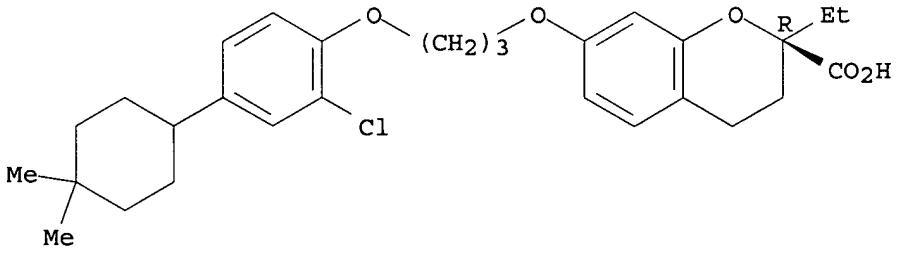
RN 444341-60-0 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[2-chloro-4-(tetrahydro-2H-pyran-4-yl)phenoxy]propoxy]-2-ethyl-3,4-dihydro-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



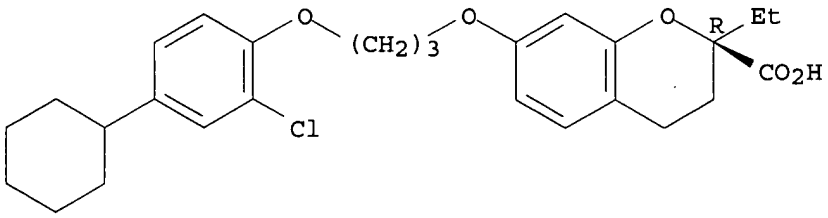
RN 444341-62-2 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[2-chloro-4-(4,4-dimethylcyclohexyl)phenoxy]propoxy]-2-ethyl-3,4-dihydro-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



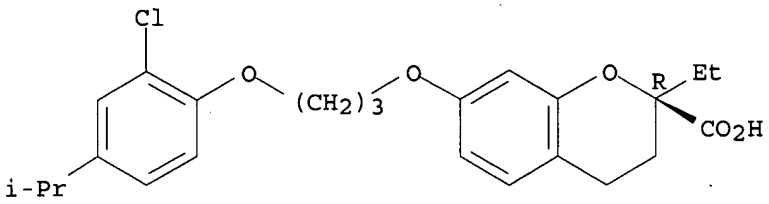
RN 444341-63-3 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(2-chloro-4-cyclohexylphenoxy)propoxy]-2-ethyl-3,4-dihydro-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



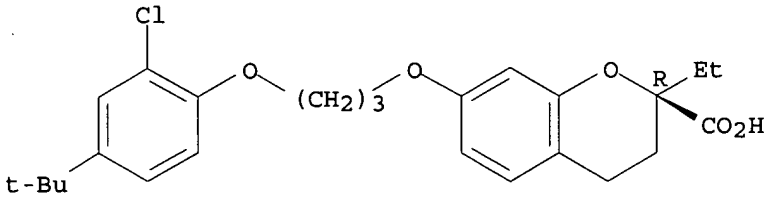
RN 444341-64-4 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[2-chloro-4-(1-methylethyl)phenoxy]propoxy]-2-ethyl-3,4-dihydro-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



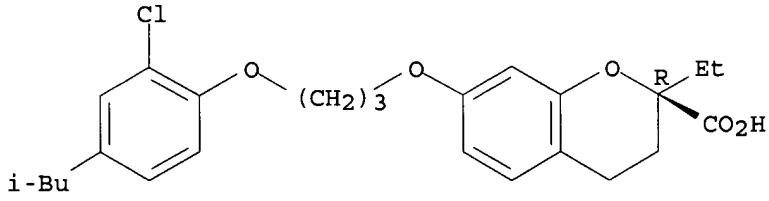
RN 444341-65-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[2-chloro-4-(1,1-dimethylethyl)phenoxy]propoxy]-2-ethyl-3,4-dihydro-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



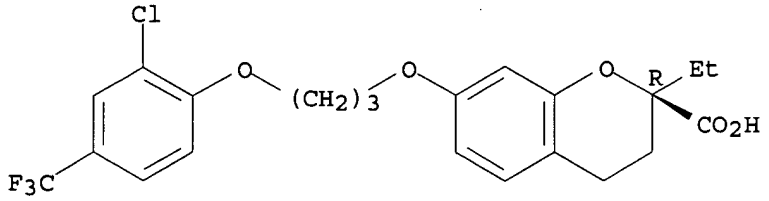
RN 444341-66-6 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[2-chloro-4-(2-methylpropyl)phenoxy]propoxy]-2-ethyl-3,4-dihydro-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



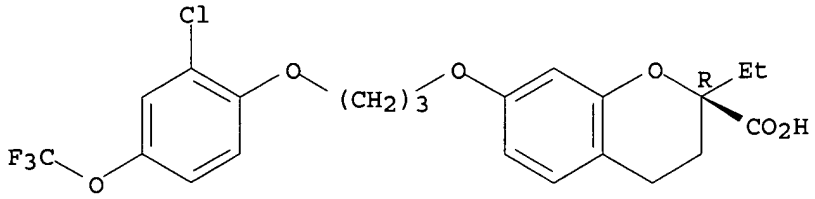
RN 444341-67-7 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[2-chloro-4-(trifluoromethyl)phenoxy]propoxy]-2-ethyl-3,4-dihydro-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



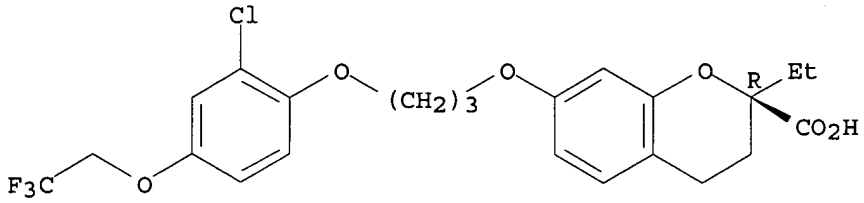
RN 444341-68-8 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[2-chloro-4-(trifluoromethoxy)phenoxy]propoxy]-2-ethyl-3,4-dihydro-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



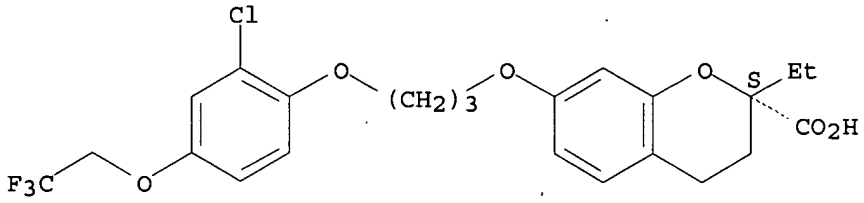
RN 444341-69-9 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[2-chloro-4-(2,2,2-trifluoroethoxy)phenoxy]propoxy]-2-ethyl-3,4-dihydro-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



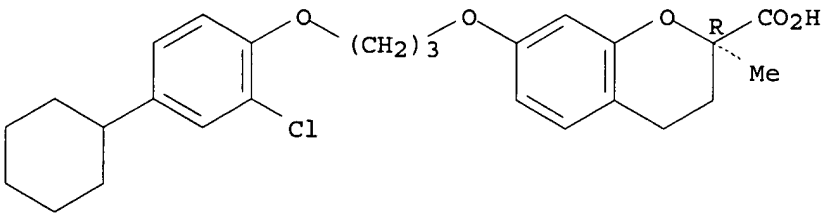
RN 444341-70-2 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[2-chloro-4-(2,2,2-trifluoroethoxy)phenoxy]propoxy]-2-ethyl-3,4-dihydro-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



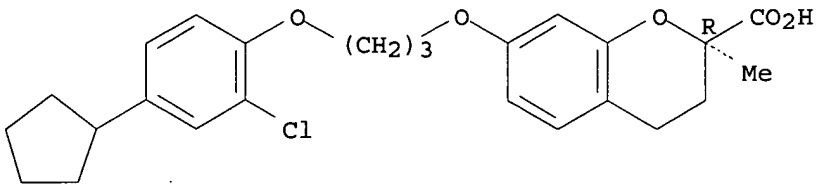
RN 444341-71-3 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(2-chloro-4-cyclohexylphenoxy)propoxy]-3,4-dihydro-2-methyl-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



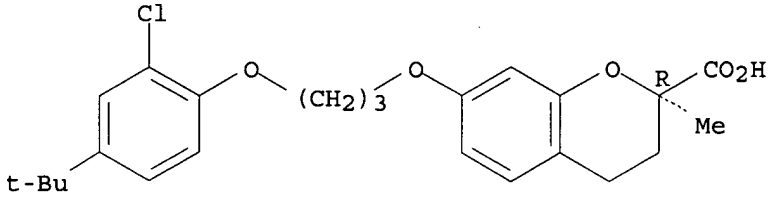
RN 444341-72-4 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(2-chloro-4-cyclopentylphenoxy)propoxy]-3,4-dihydro-2-methyl-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



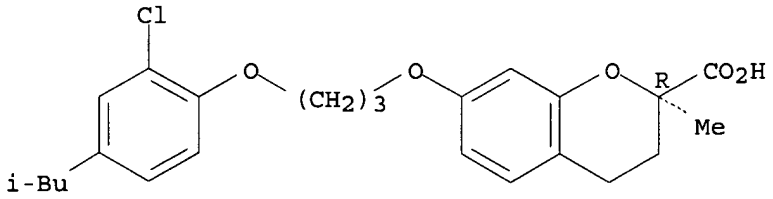
RN 444341-73-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[2-chloro-4-(1,1-dimethylethyl)phenoxy]propoxy]-3,4-dihydro-2-methyl-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



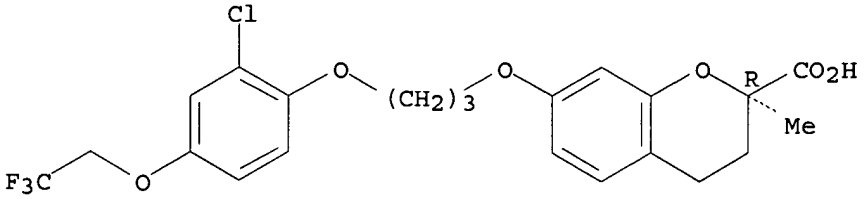
RN 444341-74-6 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[2-chloro-4-(2-methylpropyl)phenoxy]propoxy]-3,4-dihydro-2-methyl-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



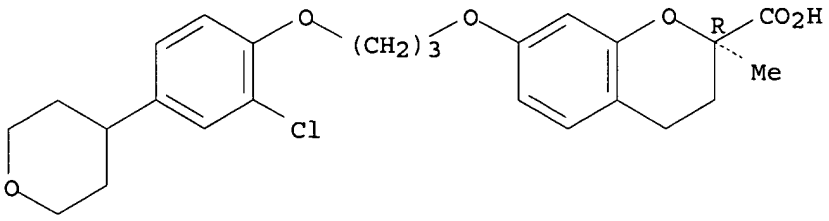
RN 444341-75-7 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[2-chloro-4-(2,2,2-trifluoroethoxy)phenoxy]propoxy]-3,4-dihydro-2-methyl-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



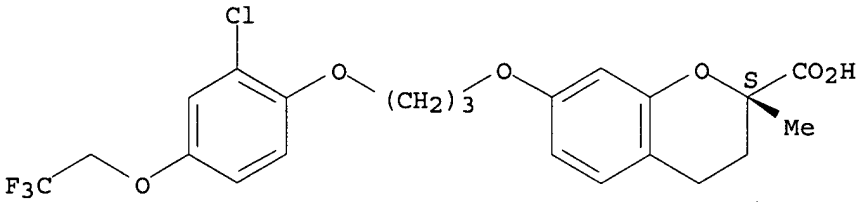
RN 444341-76-8 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[2-chloro-4-(tetrahydro-2H-pyran-4-yl)phenoxy]propoxy]-3,4-dihydro-2-methyl-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 444341-77-9 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[2-chloro-4-(2,2,2-trifluoroethoxy)phenoxy]propoxy]-3,4-dihydro-2-methyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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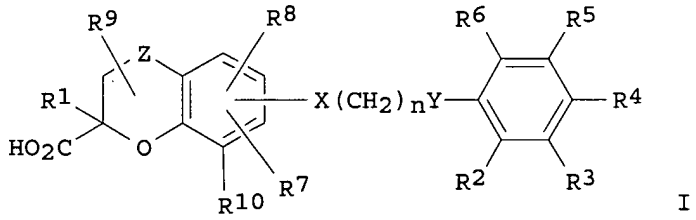

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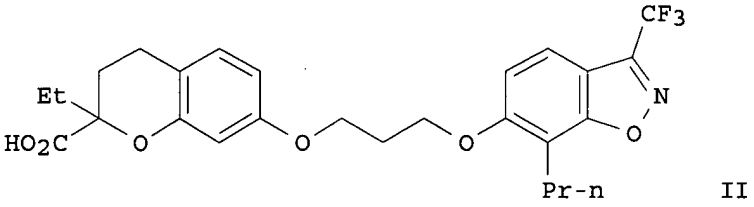


II

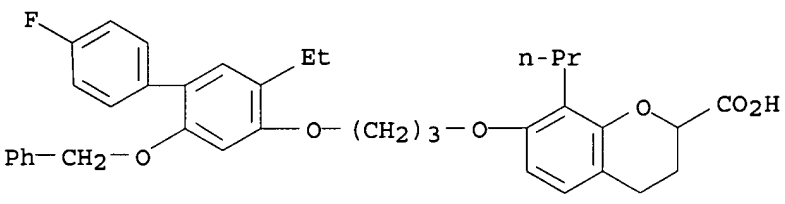
AB A class of benzopyrancarboxylic acid derivs. is disclosed, which comprises compds. that are potent agonists (no data) of peroxisome proliferator activated receptors (PPAR) alpha and/or gamma, and are therefore useful in the treatment, control, or prevention of non-insulin dependent diabetes mellitus (NIDDM), hyperglycemia, dyslipidemia, hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, atherosclerosis, obesity, vascular restenosis, inflammation, and other PPAR alpha and/or gamma mediated **diseases**, **disorders** and **conditions**.
In particular, compds. I and their pharmaceutically acceptable salts and/or prodrugs are disclosed [wherein: Z = CH2, CO; R1 = H, OH, halo, (un)substituted alk(en/yn)yl, alk(en/yn)yloxy, or aryl; or R1 forms

(un)substituted cyclopropane fusion to adjacent C atom; X, Y = O, S, SO, SO2, CH2, (un)substituted NH; n = 1-6; R4 = (un)substituted benzoheterocyclyl, cycloalkyl, heterocyclyl, cycloalkyloxy, halo, OH or derivs., alk(en/yn)yl, alk(en/yn)yloxy, or aryl, etc.; other R groups = H, halo, OH, (un)substituted alk(en/yn)yl, alk(en/yn)yloxy, aryl, aryloxy, aroyl, etc.; or R3R4 or R4R5 = (un)substituted 5- or 6-membered heterocyclic ring]. A list of 29 compds. is claimed, and their prepn. is described. For example, Et 7-hydroxy-4-oxo-4H-chromene-2-carboxylate underwent a sequence of: (1) complete hydrogenation of the enone (98%), (2) etherification of the alc. with PhCH2O(CH2)3Br (66%), (3) alpha ethylation of the ester (70%), (4) hydrogenolytic debenzylation (100%), (5) conversion of the resultant alc. to a bromide (96%), (6) etherification of the bromide with 3-(trifluoromethyl)-7-propyl-6-hydroxybenz[4,5]isoxazole (85%), and (7) alk. hydrolysis (100%), to give title compd. II. PPAR binding assays using human recombinant PPAR are described without data. Co-administration of compds. I with a variety of other drug categories, including a no. of specific drugs, is claimed.

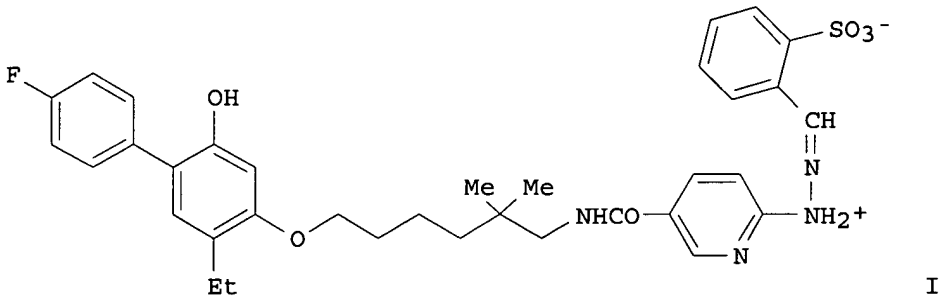
L4 ANSWER 5 OF 48 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:516582 CAPLUS
DOCUMENT NUMBER: 137:87495
TITLE: Radiopharmaceuticals for imaging infection and inflammation
INVENTOR(S): Barrett, John A.; Cheesman, Edward H.; Harris, Thomas D.; Liu, Shuang; Rajopadhye, Milind; Sworin, Michael
PATENT ASSIGNEE(S): Bristol-Myers Squibb Pharma Company, USA
SOURCE: U.S., 128 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6416733	B1	20020709	US 1997-943659	19971003

PRIORITY APPLN. INFO.: US 1996-27955P P 19961007
OTHER SOURCE(S): MARPAT 137:87495
IT **206268-03-3**, 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[[5-ethyl-4'-fluoro-2-(phenylmethoxy)[1,1'-biphenyl]-4-yl]oxy]propoxy]-3,4-dihydro-8-propyl-
RL: RCT (Reactant); RACT (Reactant or reagent)
(for prepn. of leukotriene antagonist ligands and their 99mTc complexes for imaging and treatment of infection and inflammation)
RN 206268-03-3 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[[5-ethyl-4'-fluoro-2-(phenylmethoxy)[1,1'-biphenyl]-4-yl]oxy]propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



GI



I

AB The present invention provides novel radiopharmaceuticals useful for the diagnosis of infection and inflammation, reagents and kits useful for prepg. the radiopharmaceuticals, methods of imaging sites of infection and/or inflammation in a patient, and methods of diagnosing **diseases** assocd. with infection or inflammation in patients in need of such diagnosis. The radiopharmaceuticals bind in vivo to the leukotriene B4 (LTB4) receptor on the surface of leukocytes which accumulate at the site of infection and inflammation. The reagents provided by this invention are also useful for the treatment of **diseases** assocd. with infection and inflammation. Thus, the leukotriene antagonist (I) was prepd. and shown to be active in an LTB4 human neutrophil (PMN) binding assay. Compd. I was used to prep. 99mTc(tricine)(TPPTS)(4-ethyl-2-(4-fluorophenyl)-[5-[5,5-dimethyl-6-[[[6-diazenido-3-pyridinyl]carbonyl]amino]hexyl]oxy]phenol) (TPPTS = tri(3-sulfonatophenyl)phosphine, sodium salt) which was used to detect inflammation/infection in guinea pig and rabbit focal infection models.

REFERENCE COUNT: 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 48 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:256251 CAPLUS
DOCUMENT NUMBER: 136:279341
TITLE: Praparation of benzopyrancarboxylic acid derivatives for the treatment of diabetes and lipid **disorders**
INVENTOR(S): Sahoo, Soumya P.; Koyama, Hiroo; Miller, Daniel J.; Boueres, Julia K.; Desai, Ranjit C.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 87 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002026729	A2	20020404	WO 2001-US29456	20010921
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001092874	A5	20020408	AU 2001-92874	20010921
US 2002082292	A1	20020627	US 2001-961841	20010924

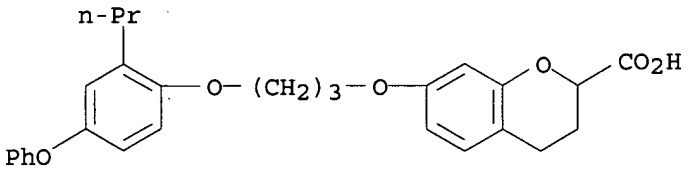
PRIORITY APPLN. INFO.: US 2000-235708P P 20000927

US 2000-244697P P 20001031
WO 2001-US29456 W 20010921

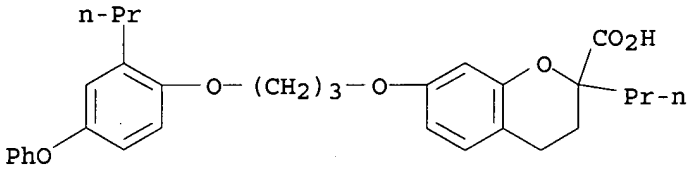
OTHER SOURCE(S): MARPAT 136:279341

IT **406488-39-9P 406488-40-2P 406488-42-4P**
406488-43-5P 406488-44-6P 406488-45-7P
406488-46-8P 406488-47-9P 406488-48-0P
406488-49-1P 406488-50-4P 406488-51-5P
406488-56-0P 406488-58-2P 406488-59-3P
406488-60-6P 406488-61-7P 406488-62-8P
406488-63-9P 406488-64-0P 406488-65-1P
406488-66-2P 406488-67-3P 406488-68-4P
406488-69-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of benzopyrancarboxylic acid derivs. for treatment of diabetes and lipid **disorders**)

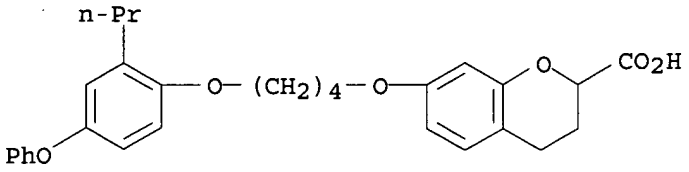
RN 406488-39-9 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 3,4-dihydro-7-[3-(4-phenoxy-2-propylphenoxy)propoxy]- (9CI) (CA INDEX NAME)



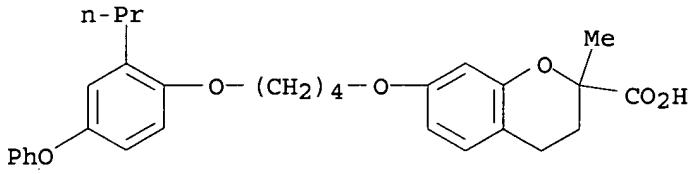
RN 406488-40-2 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 3,4-dihydro-7-[3-(4-phenoxy-2-propylphenoxy)propoxy]-2-propyl- (9CI) (CA INDEX NAME)



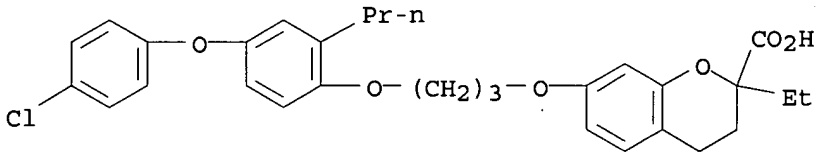
RN 406488-42-4 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 3,4-dihydro-7-[4-(4-phenoxy-2-propylphenoxy)butoxy]- (9CI) (CA INDEX NAME)



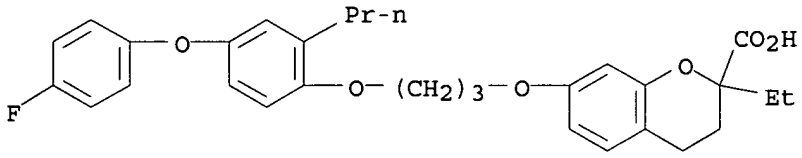
RN 406488-43-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 3,4-dihydro-2-methyl-7-[4-(4-phenoxy-2-propylphenoxy)butoxy]- (9CI) (CA INDEX NAME)



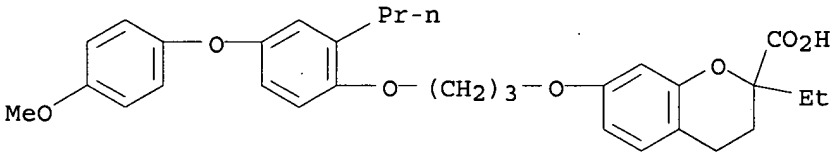
RN 406488-44-6 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[4-(4-chlorophenoxy)-2-propylphenoxy]propoxy]-2-ethyl-3,4-dihydro- (9CI) (CA INDEX NAME)



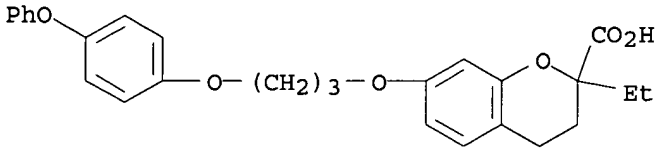
RN 406488-45-7 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 2-ethyl-7-[3-[4-(4-fluorophenoxy)-2-propylphenoxy]propoxy]-3,4-dihydro- (9CI) (CA INDEX NAME)



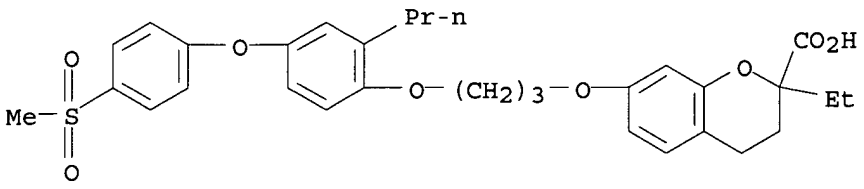
RN 406488-46-8 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 2-ethyl-3,4-dihydro-7-[3-[4-(4-methoxyphenoxy)-2-propylphenoxy]propoxy]- (9CI) (CA INDEX NAME)



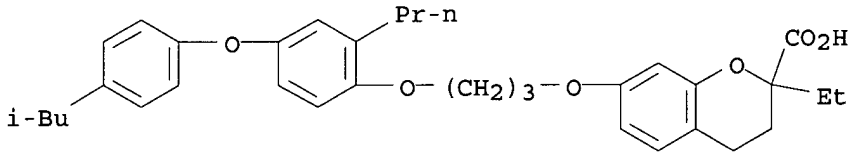
RN 406488-47-9 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 2-ethyl-3,4-dihydro-7-[3-(4-phenoxyphenoxy)propoxy]- (9CI) (CA INDEX NAME)



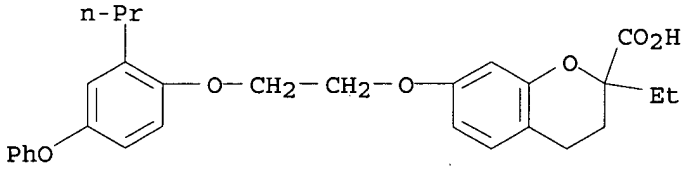
RN 406488-48-0 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 2-ethyl-3,4-dihydro-7-[3-[4-[4-(methylsulfonyl)phenoxy]-2-propylphenoxy]propoxy]- (9CI) (CA INDEX NAME)



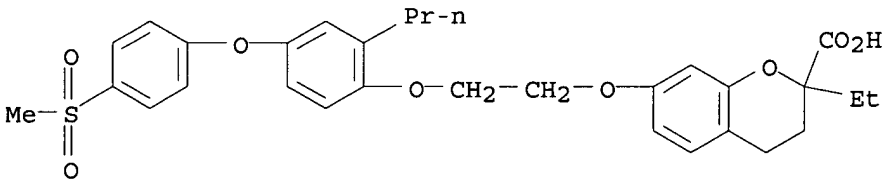
RN 406488-49-1 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 2-ethyl-3,4-dihydro-7-[3-[4-[4-(2-methylpropyl)phenoxy]-2-propylphenoxy]propoxy]- (9CI) (CA INDEX NAME)



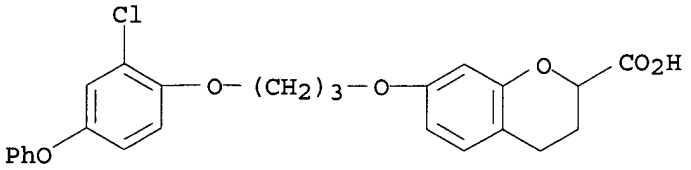
RN 406488-50-4 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 2-ethyl-3,4-dihydro-7-[2-(4-phenoxy-2-propylphenoxy)ethoxy]- (9CI) (CA INDEX NAME)



RN 406488-51-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 2-ethyl-3,4-dihydro-7-[2-[4-[4-(methylsulfonyl)phenoxy]-2-propylphenoxy]ethoxy]- (9CI) (CA INDEX NAME)

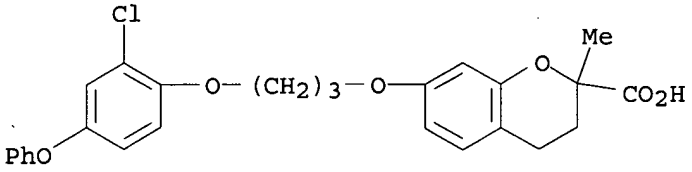


RN 406488-56-0 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(2-chloro-4-phenoxyphenoxy)propoxy]-3,4-dihydro- (9CI) (CA INDEX NAME)

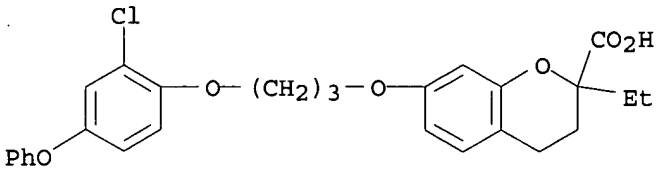


RN 406488-58-2 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(2-chloro-4-

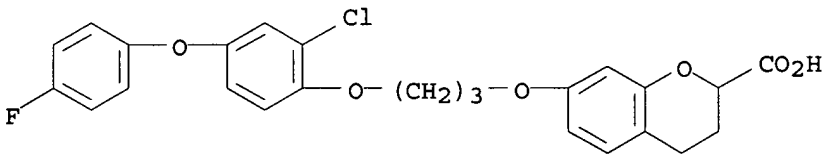
phenoxyphenoxy)propoxy]-3,4-dihydro-2-methyl- (9CI) (CA INDEX NAME)



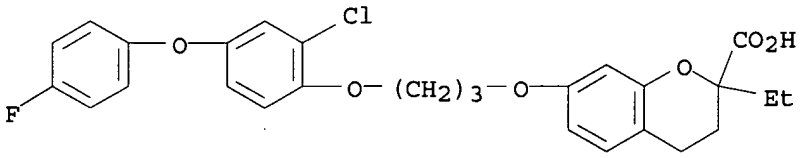
RN 406488-59-3 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(2-chloro-4-phenoxyphenoxy)propoxy]-2-ethyl-3,4-dihydro- (9CI) (CA INDEX NAME)



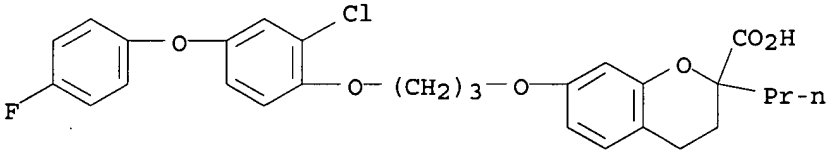
RN 406488-60-6 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[2-chloro-4-(4-fluorophenoxy)phenoxy]propoxy]-3,4-dihydro- (9CI) (CA INDEX NAME)



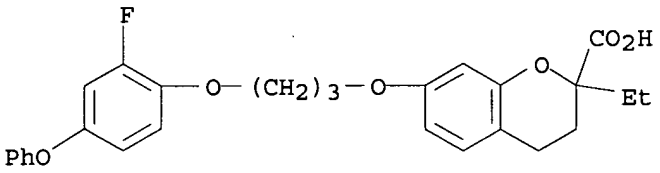
RN 406488-61-7 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[2-chloro-4-(4-fluorophenoxy)phenoxy]propoxy]-2-ethyl-3,4-dihydro- (9CI) (CA INDEX NAME)



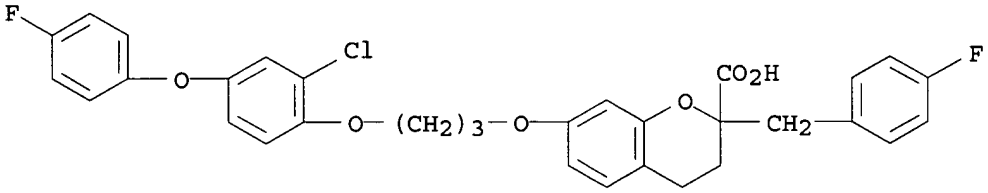
RN 406488-62-8 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[2-chloro-4-(4-fluorophenoxy)phenoxy]propoxy]-3,4-dihydro-2-propyl- (9CI) (CA INDEX NAME)



RN 406488-63-9 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 2-ethyl-7-[3-(2-fluoro-4-phenoxyphenoxy)propoxy]-3,4-dihydro- (9CI) (CA INDEX NAME)

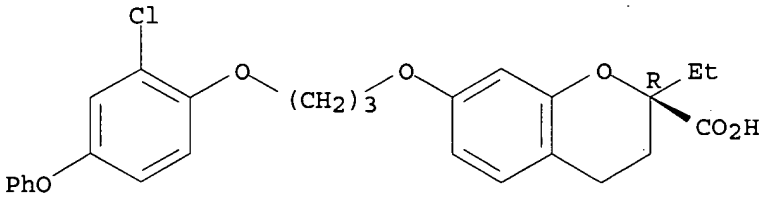


RN 406488-64-0 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[2-chloro-4-(4-fluorophenoxy)phenoxy]propoxy]-2-[(4-fluorophenyl)methyl]-3,4-dihydro- (9CI) (CA INDEX NAME)



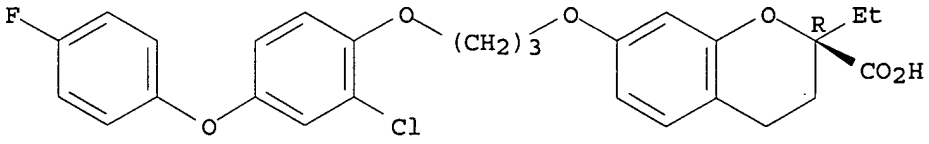
RN 406488-65-1 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(2-chloro-4-phenoxyphenoxy)propoxy]-2-ethyl-3,4-dihydro-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



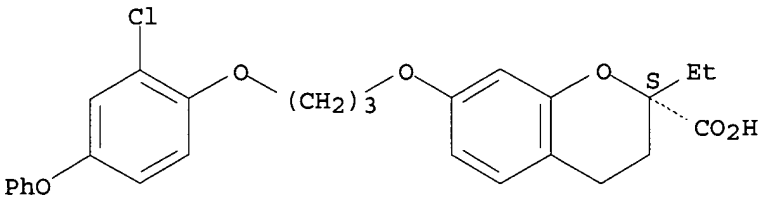
RN 406488-66-2 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[2-chloro-4-(4-fluorophenoxy)phenoxy]propoxy]-2-ethyl-3,4-dihydro-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



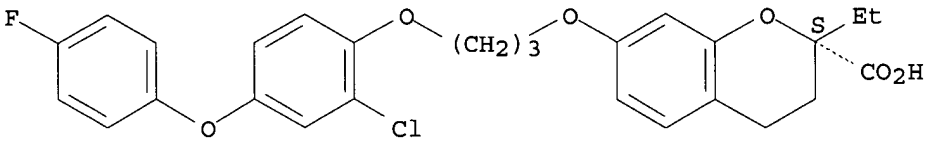
RN 406488-67-3 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(2-chloro-4-phenoxyphenoxy)propoxy]-2-ethyl-3,4-dihydro-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



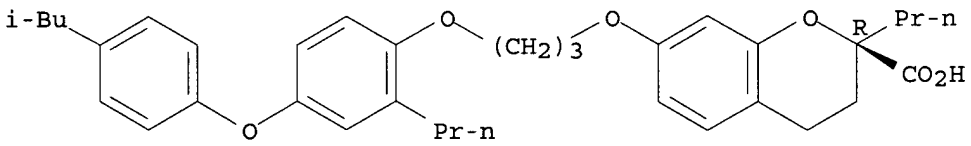
RN 406488-68-4 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[2-chloro-4-(4-fluorophenoxy)phenoxy]propoxy]-2-ethyl-3,4-dihydro-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

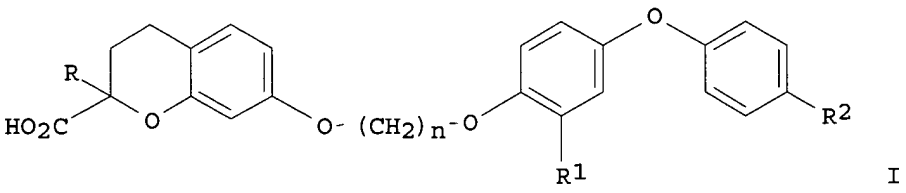


RN 406488-69-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 3,4-dihydro-7-[3-[4-[4-(2-methylpropyl)phenoxy]-2-propylphenoxy]propoxy]-2-propyl-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



GI



AB Title compds. [I; R = H, CH3CH2, CH3(CH2)2; R1 = CH3(CH2)2, Cl, F; R2 = H, F, (CH3)2CHCH2, Cl, OCH3, CH3SO2; n = 2, 3, 4], pharmaceutically acceptable salts, and stereoisomers are prepd. Title compds. I, with effective amt. of one or more compds. selected from the group consisting of glitazones, tolbutamide, lovastatin, etc., are potent agonists of PPAR alpha and/or gamma, and are therefore useful in the treatment, control or prevention of non-insulin dependent diabetes mellitus (NIDDM), hyperglycemia, dyslipidemia, hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, atherosclerosis, obesity, vascular restenosis, inflammation, and other PPAR alpha and/or gamma mediated **diseases**, **disorders** and **conditions**.

L4 ANSWER 7 OF 48 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:372369 CAPLUS

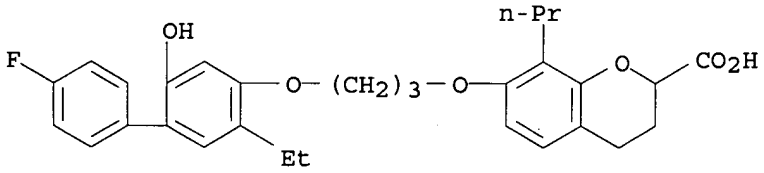
DOCUMENT NUMBER: 134:366684
TITLE: Preparation of [(phenoxyalkoxy)phenoxy]benzoates and analogs for reversal of multidrug resistance
INVENTOR(S): Jedlitschky, Gabriele; Leier, Inka; Keppler, Dietrich
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: U.S., 28 pp., Cont.-in-part of U.S. 5,543,428.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6235785	B1	20010522	US 1997-793659	19970226
US 5543428	A	19960806	US 1994-298644	19940831
DE 4432563	A1	19960314	DE 1994-4432563	19940913
DE 4432563	C2	19970724		
WO 9606604	A2	19960307	WO 1995-US11125	19950831
WO 9606604	A3	19960801		
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 2002010213	A1	20020124	US 2001-836429	20010417
US 2002013370	A1	20020131	US 2001-836567	20010417

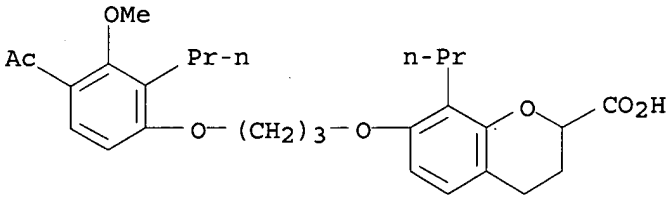
PRIORITY APPLN. INFO.:
US 1994-298644 A2 19940831
DE 1994-4432563 A 19940913
WO 1995-US11125 W 19950831
US 1997-793659 A1 19970226

OTHER SOURCE(S): MARPAT 134:366684

IT **152608-30-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of [(phenoxyalkoxy)phenoxy]benzoic acids and analogs for identification and treatment of multi-drug resistant tumors)
RN 152608-30-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[(5-ethyl-4'-fluoro-2-hydroxy[1,1'-biphenyl]-4-yl)oxy]propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



IT **120072-59-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of [(phenoxyalkoxy)phenoxy]benzoic acids and analogs for identification and treatment of multi-drug resistant tumors)
RN 120072-59-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



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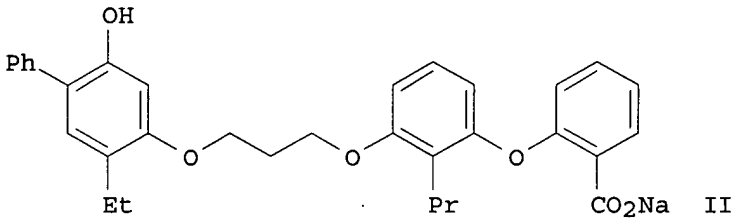


II

AB R1Z1O(CH2)nOZOR [I; R = (un)substituted C6H4CO2H; R1 = (halo)phenyl; Z = 2-(un)substituted 1,3-phenylene; Z1 = 3-alkyl-(un)substituted 1,4-phenylene; n = 3-5] were prepd. Thus, 2,6-(HO)2C6H3Pr was etherified by 2-IC6H4CO2Me and the product etherified by PhZ1O(CH2)3Cl (Z1 = 6-benzyloxy-3-ethyl-1,4-phenylene) to give, in 2 addnl. steps, title compd. II. Data for biol. activity of I were given.

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 48 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:209933 CAPLUS
DOCUMENT NUMBER: 132:246369
TITLE: Use of non-peptidyl compounds for the treatment of insulin-related ailments
INVENTOR(S): Helmerhorst, Erik; Plewright, Brian Scott
PATENT ASSIGNEE(S): Curtin University of Technology, Australia
SOURCE: PCT Int. Appl., 129 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000016798	A1	20000330	WO 1999-AU786	19990917
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9960707	A1	20000410	AU 1999-60707	19990917
EP 1115422	A1	20010718	EP 1999-947113	19990917
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: AU 1998-6091 A 19980922
WO 1999-AU786 W 19990917

OTHER SOURCE(S): MARPAT 132:246369

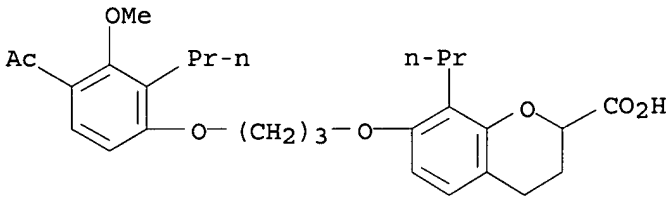
IT **120072-59-5 147612-00-8 152608-30-5 156005-27-5 156005-50-4**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(non-peptidyl compds. modulating insulin activity by mimicking amino acid residues spatially located on insulin and binding to insulin receptors)

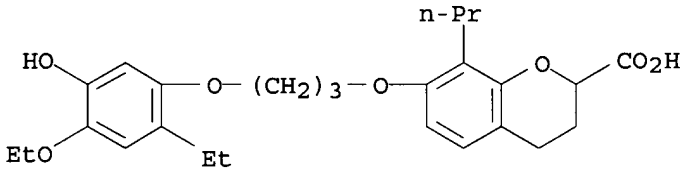
RN 120072-59-5 CAPLUS

CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



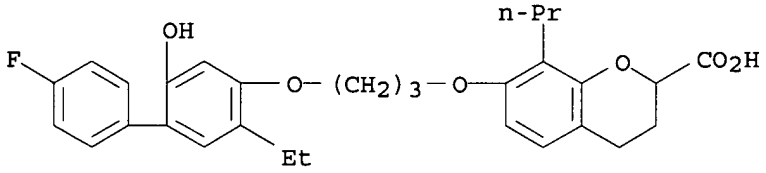
RN 147612-00-8 CAPLUS

CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-ethoxy-2-ethyl-5-hydroxyphenoxy)propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



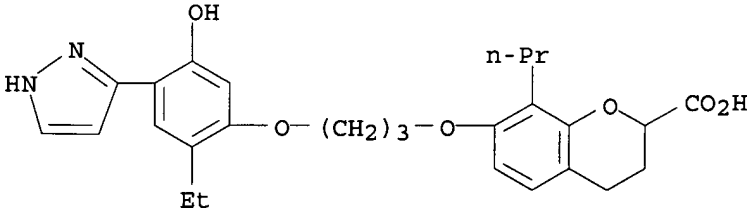
RN 152608-30-5 CAPLUS

CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[(5-ethyl-4'-fluoro-2-hydroxy[1,1'-biphenyl]-4-yl)oxy]propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)

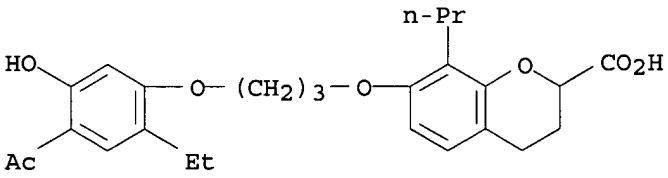


RN 156005-27-5 CAPLUS

CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[2-ethyl-5-hydroxy-4-(1H-pyrazol-3-yl)phenoxy]propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



RN 156005-50-4 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-2-ethyl-5-hydroxyphenoxy)propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



AB The present invention relates to the use of at least a non-peptidyl compd. as a biol. modulator of insulin activity or insulin-related activity for the treatment of insulin-related **diseases**. Non-peptidyl compds. of the present invention exert their effects by mimicking amino acids spatially located on insulin, enabling those compds. to bind to the insulin receptor or insulin-like receptor causing biol. modulation of the activity of the receptor. A method for identifying a non-peptidyl compd. comprises the steps of: (1) comparing the 3D structure of the non-peptidyl compd. with a 3D pharmacophore of an active site of insulin, and (2) selecting a non-peptidyl compd. The compds. may act either as agonists or antagonists of insulin or insulin-like activity. Pharmaceutical compns. contg. chem. compds. capable of modulating the biol. activity of insulin are also claimed. For example, 4,4'-methylenebis[3-hydroxy-2-naphthalenecarboxylic acid] (IM 025) was an antagonist of insulin action. IM 025 caused a dose-dependent decrease in the incorporation of 32P into FYF peptide in insulin-stimulated tubes and inhibited glucose transport in 3T3L1 cells, with IC50 of 150 and 170 .mu.M, resp. 2,4-Dichloro-6-[N-(trifluoromethanesulfonyl)sulfamoylphenyl-3,5-dichloro-2-hydroxybenzene] sulfonate (IM 103) was an agonist of insulin action displaying a biphasic biol. dose response curve with an apex at concn. of 110 .mu.M and an apparent EC50 of 45 .+-. 7 .mu.M.

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 48 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:239130 CAPLUS
DOCUMENT NUMBER: 128:303347
TITLE: Radiopharmaceuticals for imaging infection and inflammation
INVENTOR(S): Barrett, John Andrew; Cheesman, Edward Hollister; Harris, Thomas David; Rajopadhye, Milind
PATENT ASSIGNEE(S): Du Pont Merck Pharmaceutical Company, USA
SOURCE: PCT Int. Appl., 352 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9815295	A2	19980416	WO 1997-US18096	19971006
WO 9815295	A3	19980827		
W: AM, AU, AZ, BR, BY, CA, CN, CZ, EE, HU, IL, JP, KG, KR, KZ, LT, LV, MD, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, UA, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9852381	A1	19980505	AU 1998-52381	19971006
AU 736481	B2	20010726		
BR 9712281	A	19990831	BR 1997-12281	19971006
CN 1239895	A	19991229	CN 1997-180342	19971006

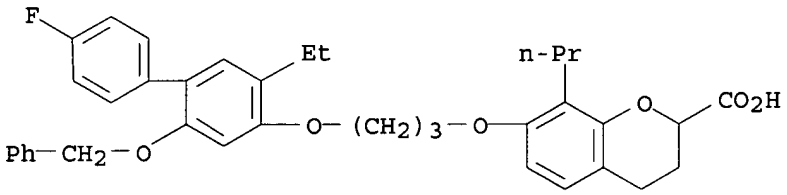
EP 999856 A2 20000517 EP 1997-947259 19971006
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI
JP 2001525796 T2 20011211 JP 1998-517680 19971006
ZA 9708956 A 19990416 ZA 1997-8956 19971007
KR 2000048922 A 20000725 KR 1999-702953 19990406
PRIORITY APPLN. INFO.: US 1996-726507 A 19961007
WO 1997-US18096 W 19971006

OTHER SOURCE(S): MARPAT 128:303347

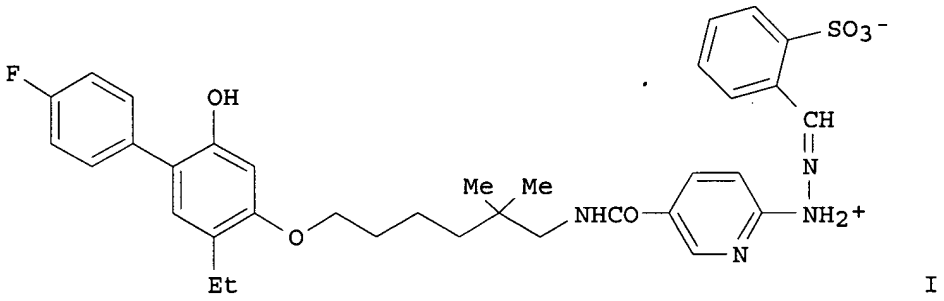
IT **206268-03-3**
RL: RCT (Reactant); RACT (Reactant or reagent)
(for prepn. of leukotriene antagonist ligands and their 99mTc complexes for imaging and treatment of infection and inflammation)

RN 206268-03-3 CAPLUS

CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[[5-ethyl-4'-fluoro-2-(phenylmethoxy)[1,1'-biphenyl]-4-yl]oxy]propoxy]-3,4-dihydro-8-propyl-(9CI) (CA INDEX NAME)



GI



I

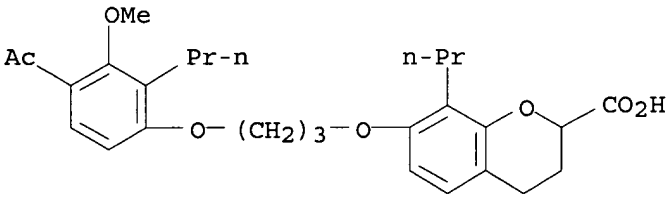
AB The present invention provides novel radiopharmaceuticals useful for the diagnosis of infection and inflammation, reagents and kits useful for prepg. the radiopharmaceuticals, methods of imaging sites of infection and/or inflammation in a patient, and methods of diagnosing **diseases** assocd. with infection or inflammation in patients in need of such diagnosis. The radiopharmaceuticals bind in vivo to the leukotriene B4 (LTB4) receptor on the surface of leukocytes which accumulate at the site of infection and inflammation. The reagents provided by this invention are also useful for the treatment of **diseases** assocd. with infection and inflammation. Thus, the leukotriene antagonist (I) was prepd. and shown to be active in an LTB4 human neutrophil (PMN) binding assay. Compd. I was used to prep. 99mTc(tricine)(TPPTS)(4-ethyl-2-(4-fluorophenyl)-[5-[5,5-dimethyl-6-[[[6-diazenido-3-pyridinyl]carbonyl]amino]hexyl]oxy]phenol) (TPPTS = tri(3-sulfonatophenyl)phosphine, sodium salt) which was was used to detect inflammation/infection in guinea pig and rabbit focal infection models.

L4 ANSWER 10 OF 48 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:557660 CAPLUS

DOCUMENT NUMBER: 127:239120
TITLE: Compositions comprising a cyclooxygenase-2 inhibitor and a leukotriene B4 receptor antagonist for reducing transplant rejection
INVENTOR(S): Gregory, Susan A.; Isakson, Peter C.; Anderson, Gary
PATENT ASSIGNEE(S): G.D. Searle & Co., USA; Gregory, Susan A.; Isakson, Peter C.; Anderson, Gary
SOURCE: PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

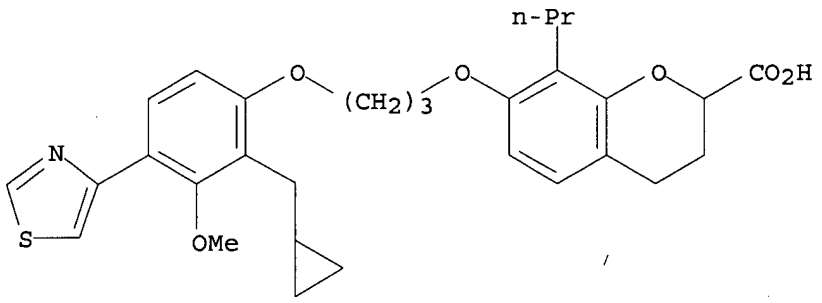
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9729775	A1	19970821	WO 1997-US1422	19970211
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2246356	AA	19970821	CA 1997-2246356	19970211
AU 9722500	A1	19970902	AU 1997-22500	19970211
EP 880362	A1	19981202	EP 1997-905663	19970211
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 2000505445	T2	20000509	JP 1997-529359	19970211
US 6172096	B1	20010109	US 1998-75633	19980511

PRIORITY APPLN. INFO.: US 1996-600580 A1 19960213
WO 1997-US1422 W 19970211
OTHER SOURCE(S): MARPAT 127:239120
IT **120072-59-5**, SC-41930 **162153-46-0**, SC 52798
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. comprising a cyclooxygenase-2 inhibitor and a leukotriene B4 receptor antagonist for reducing transplant rejection)
RN 120072-59-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



RN 162153-46-0 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[2-(cyclopropylmethyl)-3-methoxy-4-(4-thiazolyl)phenoxy]propoxy]-3,4-dihydro-8-propyl-, (+)- (9CI) (CA INDEX NAME)

Rotation (+).

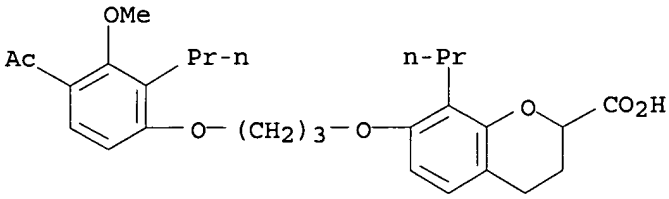


AB Treatment with a cyclooxygenase-2 inhibitor and a leukotriene B4 receptor antagonist is described as being useful in reducing recipient rejection of transplanted organs and for treatment of autoimmune **diseases**.

L4 ANSWER 11 OF 48 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:175052 CAPLUS
DOCUMENT NUMBER: 126:166481
TITLE: Combination of a cyclooxygenase-2 inhibitor and a leukotriene B4 receptor antagonist for the treatment of inflammations
INVENTOR(S): Isakson, Peter C.; Anderson, Gary D.; Gregory, Susan A.
PATENT ASSIGNEE(S): G.D. Searle & Co., USA
SOURCE: PCT Int. Appl., 72 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9641645	A1	19961227	WO 1996-US9905	19960611
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN				
CA 2224563	AA	19961227	CA 1996-2224563	19960611
AU 9662694	A1	19970109	AU 1996-62694	19960611
EP 833664	A1	19980408	EP 1996-921477	19960611
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 11507669	T2	19990706	JP 1996-503237	19960611

PRIORITY APPLN. INFO.: US 1995-489415 A 19950612
WO 1996-US9905 W 19960611
OTHER SOURCE(S): MARPAT 126:166481
IT **120072-59-5**, SC-41930
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination of a cyclooxygenase-2 inhibitor and a leukotriene B4 receptor antagonist for treatment of inflammation)
RN 120072-59-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)

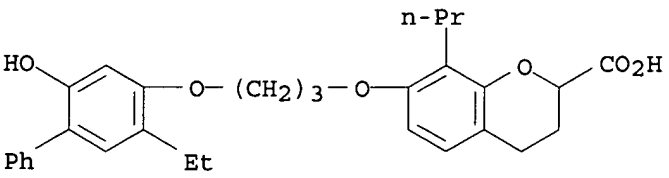


AB Combinations of a cyclooxygenase-2 inhibitor and a leukotriene B4 receptor antagonist are described for treatment of inflammation and inflammation-related **disorders**. The cyclooxygenase-2 inhibitors were prepd. Also, formulations for the drug combination are described.

L4 ANSWER 12 OF 48 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:53684 CAPLUS
DOCUMENT NUMBER: 126:74591
TITLE: Preparation of biphenylyloxyalkylarenes as leukotriene antagonists for the treatment or prevention of Alzheimer's **disease**.
INVENTOR(S): Altstiel, Larry Douglas; Fleisch, Jerome Herbert
PATENT ASSIGNEE(S): Lilly, Eli, and Co., USA
SOURCE: Eur. Pat. Appl., 124 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

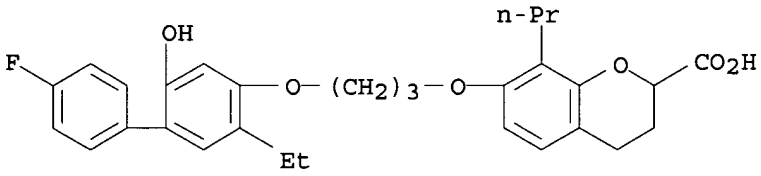
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 743064	A1	19961120	EP 1996-303346	19960513
R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
WO 9636347	A1	19961121	WO 1996-US6773	19960513
W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM				
RW: KE, LS, MW, SD, SZ, UG, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9658572	A1	19961129	AU 1996-58572	19960513

PRIORITY APPLN. INFO.: US 1995-443179 19950517
WO 1996-US6773 19960513
OTHER SOURCE(S): MARPAT 126:74591
IT **152608-29-2P 152608-30-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of biphenylyloxyalkylarenes as leukotriene antagonists for the treatment or prevention of Alzheimer's **disease**)
RN 152608-29-2 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[(5-ethyl-2-hydroxy[1,1'-biphenyl]-4-yl)oxy]propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)

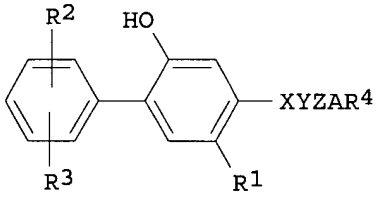


RN 152608-30-5 CAPLUS

CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[(5-ethyl-4'-fluoro-2-hydroxy[1,1'-biphenyl]-4-yl)oxy]propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



GI



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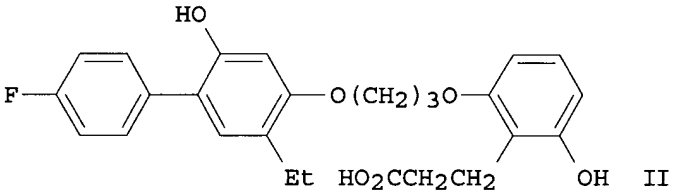


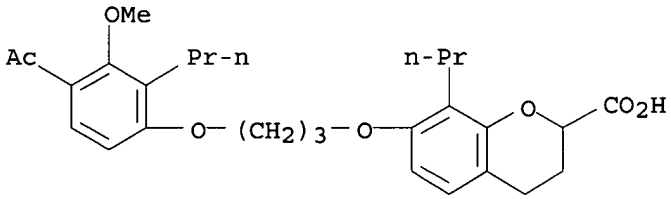
II

AB Use of compds. having leukotriene antagonist activity, e.g., title compds. [I; R1 = alkyl, alkenyl, alkynyl, alkoxy, alkylthio, halo, R2-substituted Ph; R2, R3 = H, halo, OH, alkyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, CF3, dialkylamino; X = O, S, CO, CH2; Y = O, CH2; XY = CH:CH, C.tplbond.C; Z = alkylene; A = bond, O, S, CH:CH, etc.; R4 = (substituted) (hetero)aryl; with provisos] for manuf. of a medicament for treating or preventing Alzheimer's **disease** is claimed. Thus, 5-hydroxybenzopyran-2-one and 3-(2-ethyl-4-(4-fluorophenyl)-5-benzyloxyphenyl)propyl iodide were stirred with NaH in Me2SO to give 5-[3-(2-ethyl-4-(4-fluorophenyl)-5-benzyloxyphenyl)propoxy]benzopyran-2-one. This was converted to title compd. (II), which displaced [3H]-LTB4 from guinea pig lung membrane prepns. with pKi = 9.01. I drug formulations are given.

L4 ANSWER 13 OF 48 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1996:658895 CAPLUS
DOCUMENT NUMBER: 125:325054
TITLE: Study on the experimental ulcerative colitis (UC) model induced by dextran sulfate sodium (DSS) in rats. 3
AUTHOR(S): Kimura, Isami; Nagahama, Shinobu; Kawasaki, Maki; Kataoka, Mikiko; Sato, Makoto
CORPORATE SOURCE: Preclin. Dev. Lab., Nippon Hoechst Marion Roussel Ltd., Shiga, 520-23, Japan
SOURCE: Nippon Yakurigaku Zasshi (1996), 108(5), 259-266
CODEN: NYKZAU; ISSN: 0015-5691

PUBLISHER: Nippon Yakuri Gakkai
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
IT **120072-59-5**, SC-41930
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(inflammatory mediators in dextran sulfate-induced ulcerative colitis)
RN 120072-59-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



AB We have already confirmed that symptoms in the exptl. UC model in rats induced by ingesting DSS resembled those of human UC. To clarify the participation of chem. mediators concerned with the development and etiol. of the exptl. UC model, we investigated the effects of superoxide dismutase (SOD), 5-aminosalicylic acid (5-ASA), AA-861, and LTB4-receptor antagonist (LTB4-ra), indomethacin (Ind) and OKY-046 on the DSS-induced UC model in rats. The UC model was produced by giving rats drinking water contg. 3% DSS, and animals were selected when bloody stool was obsd. in more than 90% of the animals. After selection, drugs were intrarectally administered once a day, for 7 days, to UC rats that were given drinking water contg. 1% DSS. SOD, 5-ASA, AA-861 and LTB4-ra inhibited the formation of erosions in the large intestine. Furthermore, SOD, 5-ASA and LTB4-ra improved the length of the large intestine of rats that had been shortened by ingesting DSS. On the other hand, neither Ind nor OKY-046 improved the shortening and erosion of the large intestine. From these results, it is concluded that the free radical and lipoxygenase metabolites of arachidonic acid may be partially involved in the DSS-induced UC model in rats.

L4 ANSWER 14 OF 48 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:194704 CAPLUS
DOCUMENT NUMBER: 124:260839
TITLE: Leukotriene B4 antagonists
INVENTOR(S): Djuric, Stevan Wakefield; Yu, Stella Siu-Tzyy
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9533742	A1	19951214	WO 1995-US6702	19950531
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5516917	A	19960514	US 1994-255275	19940608

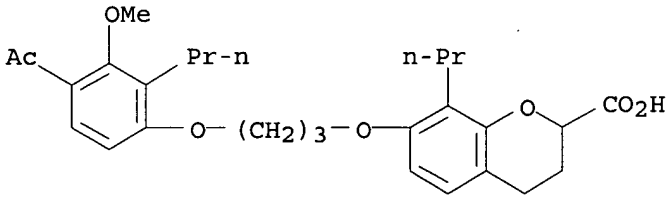
AU 9526523 A1 19960104 AU 1995-26523 19950531
US 5684162 A 19971104 US 1996-605732 19960222
PRIORITY APPLN. INFO.: US 1994-255275 19940608
WO 1995-US6702 19950531

OTHER SOURCE(S): MARPAT 124:260839

IT **120072-59-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 120072-59-5 CAPLUS

CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



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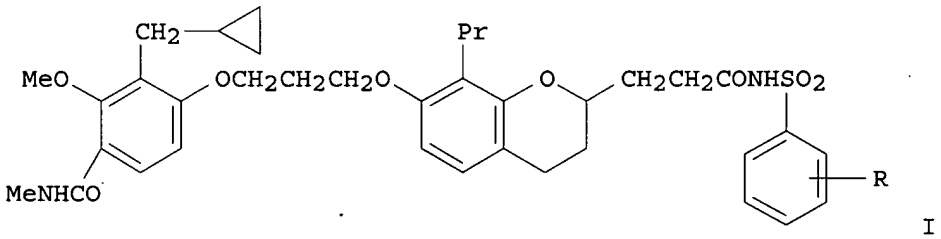


I

AB The title compds. I (R = H, o-, p-Me) were prepd. by amidation of the propionic acid deriv. with RC6H4SO2NH2. Compds. I are leukotriene B4 antagonists and are useful as anti-inflammatory agents and in treating **disease conditions** mediated by LTB4.

L4 ANSWER 15 OF 48 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:175604 CAPLUS
DOCUMENT NUMBER: 124:232451
TITLE: Preparation of (azolylphenoxy)alkoxy-substituted dihydrobenzopyran-2-sulfonimides derivatives as leukotriene B4 antagonists
INVENTOR(S): Djuric, Stevan Wakefield; Penning, Thomas Dale
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9532201	A1	19951130	WO 1995-US5850	19950517

W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT

RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9525855	A1	19951218	AU 1995-25855	19950517
US 5578619	A	19961126	US 1995-569323	19951208
PRIORITY APPLN. INFO.:			US 1994-249107	19940525
			WO 1995-US5850	19950517

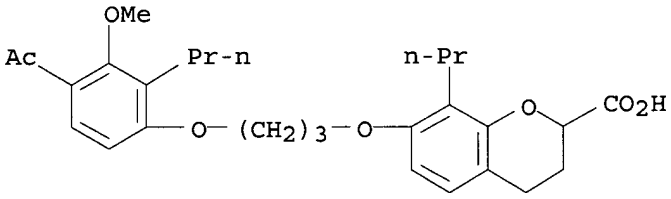
OTHER SOURCE(S): MARPAT 124:232451

IT **120072-59-5P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of [(azolylphenoxy)alkoxy]dihydrobenzopyran sulfonimide derivs. as leukotriene B4 antagonists for treating inflammatory **diseases**)

RN 120072-59-5 CAPLUS

CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)

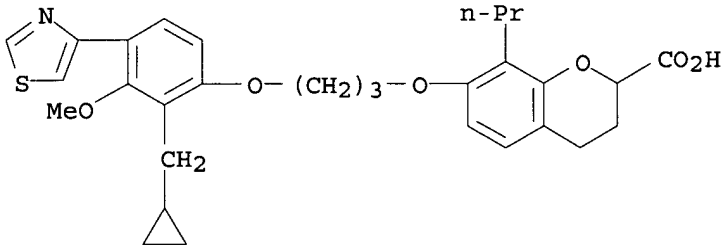


IT **138828-39-4**

RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of [(azolylphenoxy)alkoxy]dihydrobenzopyran sulfonimide derivs. as leukotriene B4 antagonists for treating inflammatory **diseases**)

RN 138828-39-4 CAPLUS

CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[2-(cyclopropylmethyl)-3-methoxy-4-(4-thiazolyl)phenoxy]propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



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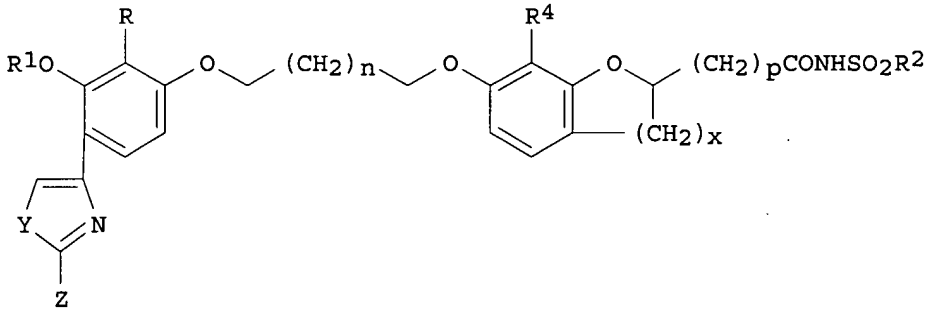

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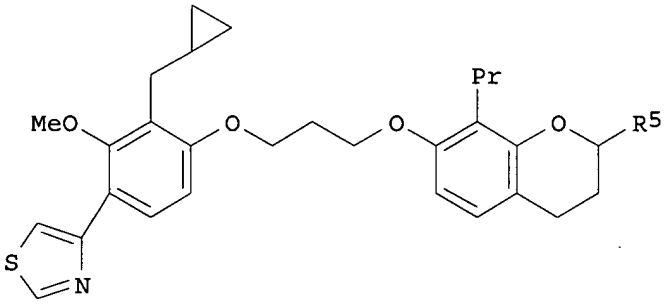


II

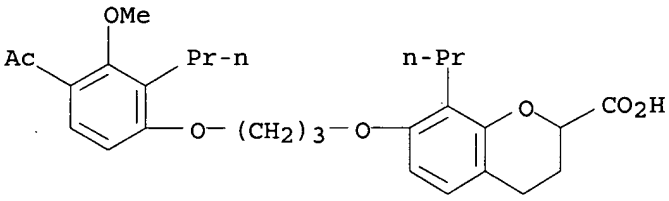
AB The title compds. [I; R = C2-6 alkyl, alkenyl, or alkynyl, (CH2)mR3; wherein R3 = C3-5 cycloalkyl; m = 1 or 2; R1 = C1-4 alkyl; R2 = C1-5 alkyl, aryl optionally substituted with halogen or C1-5 alkyl; R4 = C1-6 alkyl; n = 1-5; p = 0-6; x = 0 or 2; Y = NH, O, S; Z = H, C1-4 alkyl or alkoxy] and stereoisomers and pharmaceutically acceptable salts thereof, which are useful as antiinflammatory agents and in the treatment of leukotriene B4 mediated **conditions** such as inflammatory **diseases** including rheumatoid arthritis, psoriasis, inflammatory bowel **disease**, gout, asthma, and multiple sclerosis, are prepd. Thus, the benzopyrancarboxylic acid deriv. (II; R = CO2H) 15, PhSO2NH2 15, 4-dimethylaminopyridine 15, 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide 19 mg, and 5 mL CH2Cl2 were stirred with 4.ANG. mol. sieves at room temp. for 24 h to give, after flash chromatog., 29 mg the Ph sulfonimide II (R = CONHSO2Ph). The latter compd. and II (R = CH2CH2CONHSO2Ph) showed the leukotriene B4 receptor binding affinity 5.5 and 4.3 times, resp., greater than that of 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl-2H-1-benzopyran-2-carboxylic acid.

L4 ANSWER 16 OF 48 CAPLUS COPYRIGHT 2002 ACS

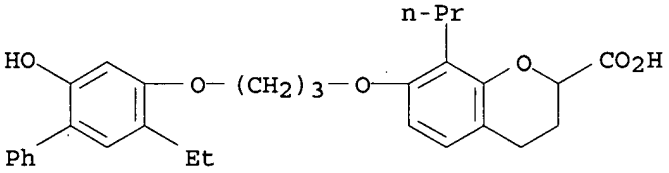
ACCESSION NUMBER:	1995:849927 CAPLUS
DOCUMENT NUMBER:	124:55467
TITLE:	Synthetic and Structure/Activity Studies on Acid-Substituted 2-Arylphenols: Discovery of 2-[2-Propyl-3-[3-[2-ethyl-4-(4-fluorophenyl)-5-hydroxyphenoxy]- propoxy]phenoxy]benzoic Acid, a High-Affinity Leukotriene B4 Receptor Antagonist
AUTHOR(S):	Sawyer, J. Scott; Bach, Nicholas J.; Baker, S. Richard; Baldwin, Ronald F.; Borromeo, Peter S.; Cockerham, Sandra L.; Fleisch, Jerome H.; Floreancig, Paul; Froelich, Larry L.; et al.
CORPORATE SOURCE:	Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN, 46285, USA
SOURCE:	Journal of Medicinal Chemistry (1995), 38(22), 4411-32 CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER:	American Chemical Society
DOCUMENT TYPE:	Journal
LANGUAGE:	English

IT **120072-59-5P 152608-29-2P 152608-30-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(structure-activity relationship of [hydroxy[[(tetrazolyl)alkyl]oxy]phenyl]ethanone derivs. and analogs)

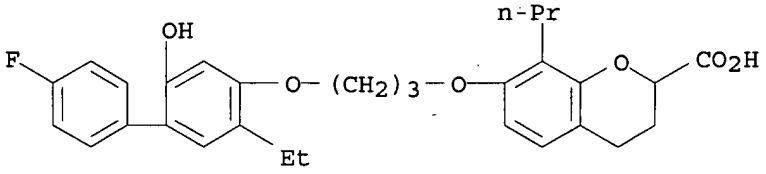
RN 120072-59-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



RN 152608-29-2 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[(5-ethyl-2-hydroxy[1,1'-biphenyl]-4-yl)oxy]propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



RN 152608-30-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[(5-ethyl-4'-fluoro-2-hydroxy[1,1'-biphenyl]-4-yl)oxy]propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



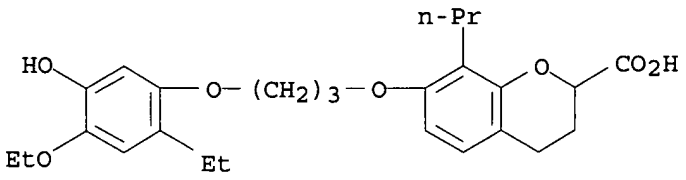
AB Structural derivs. of LY255283 have been studied as receptor antagonists of leukotriene B4. Substitution of the 2-hydroxyacetophenone subunit of 1-[5-Ethyl-2-hydroxy-4-[[6-methyl-6-(1H-tetrazol-5-yl)heptyl]oxy]phenyl]ethanone (LY255283) with a 2-arylphenol group provided entry into several new series that feature various mono- and diacidic core functionality. These new analogs, the subject of a broad structure-activity investigation, displayed significantly increased in vitro and in vivo activity as receptor antagonists of LTB4. A series of diaryl ether carboxylic acids demonstrated esp. interesting activity and led to the discovery of 2-[2-propyl-3-[3-[2-ethyl-4-(4-fluorophenyl)-5-hydroxyphenoxy]propoxy]phenoxy]benzoic acid (LY293111), a 2-arylphenol-substituted diaryl ether carboxylic acid which displayed potent binding to human neutrophils (IC50 = 17 .+-. 4.6 nM) and guinea pig lung membranes (IC50 = 6.6 .+-. 0.71 nM), inhibition of LTB4-induced expression of the CD11b/CD18 receptor on human neutrophils (IC50 = 3.3 .+-. 0.81 nM), and inhibition of LTB4-induced contraction of guinea pig lung parenchyma (pKB = 8.7 .+-. 0.16). 801Vivo, LY293111 demonstrated potent activity in inhibiting LTB4-induced airway obstruction in the

guinea pig when dosed by the oral (ED50 = 0.40 mg/kg) or i.v. (ED50 = 0.014 mg/kg) routes. A specific LTB4 receptor antagonist, LY293111 had little effect on inhibiting contractions of guinea pig lung parenchyma induced by leukotriene D4 (LTD4), histamine, carbachol, or U46619. LY293111 was chosen as a clin. candidate and is currently in phase I studies for a variety of inflammatory **diseases**.

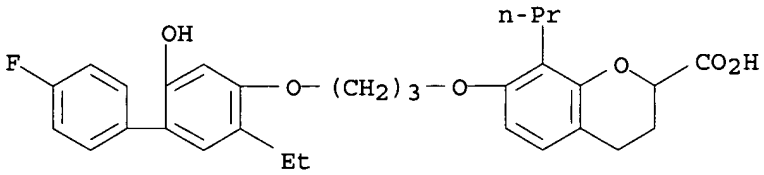
L4 ANSWER 17 OF 48 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:792781 CAPLUS
DOCUMENT NUMBER: 123:188623
TITLE: Use of PLA2 inhibitors as treatment for Alzheimers **disease**
INVENTOR(S): Clemens, James Allen; Sofia, Michael Joseph; Stepenson, Diane Teresa
PATENT ASSIGNEE(S): Lilly, Eli, and Co., USA
SOURCE: PCT Int. Appl., 91 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9517183	A1	19950629	WO 1994-US14504	19941214
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, UZ, VN				
RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5478857	A	19951226	US 1993-173544	19931223
CA 2179649	AA	19950629	CA 1994-2179649	19941214
AU 9514028	A1	19950710	AU 1995-14028	19941214
AU 688446	B2	19980312		
EP 735870	A1	19961009	EP 1995-905404	19941214
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CN 1142768	A	19970212	CN 1994-195027	19941214
HU 75335	A2	19970528	HU 1996-1741	19941214
JP 09507069	T2	19970715	JP 1994-517514	19941214
BR 9408407	A	19970805	BR 1994-8407	19941214
ZA 9410041	A	19960618	ZA 1994-10041	19941215
US 5563164	A	19961008	US 1995-464030	19950605
NO 9602568	A	19960809	NO 1996-2568	19960617
FI 9602557	A	19960822	FI 1996-2557	19960619

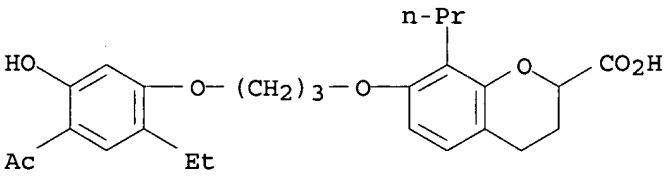
PRIORITY APPLN. INFO.: US 1993-173544 19931223
WO 1994-US14504 19941214
OTHER SOURCE(S): MARPAT 123:188623
IT **147612-00-8P 152608-30-5P 156005-50-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(phospholipase A2 inhibitors for treatment of Alzheimers **disease**)
RN 147612-00-8 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-ethoxy-2-ethyl-5-hydroxyphenoxy)propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



RN 152608-30-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[(5-ethyl-4'-fluoro-2-hydroxy[1,1'-biphenyl]-4-yl)oxy]propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



RN 156005-50-4 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-2-ethyl-5-hydroxyphenoxy)propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



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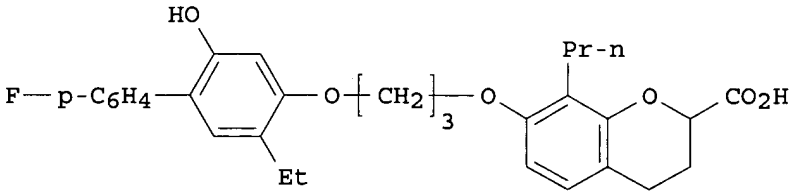
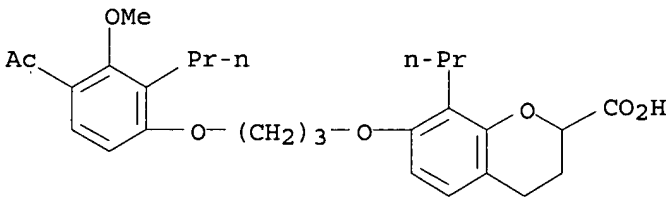


I

AB This invention provides methods for the treatment or prevention of Alzheimer's **disease** in a mammal which comprises administering to a mammal in need thereof an effective amt. of an inhibitor of phospholipase A2 (PLA2), esp. cytosolic PLA2. E.g., I was prepd. and shows good PLA2 inhibitory activity. Pharmaceutical formulations are also given.

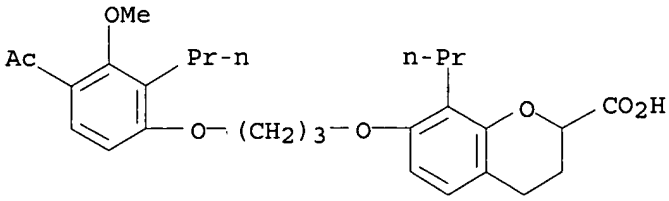
L4 ANSWER 18 OF 48 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:749667 CAPLUS
DOCUMENT NUMBER: 123:160397
TITLE: Otitis externa and anti-inflammatory activity of SC-41930, a selective leukotriene B4 receptor antagonist
AUTHOR(S): Sutbeyaz, Yavuz; Yakan, Birkan; Doner, Fehmi; Ciftcioglu, Akif
CORPORATE SOURCE: Fac. Med., Ataturk Univ., Erzurum, Turk.
SOURCE: Turkish Journal of Medical Sciences (1995), 24(2),

129-32
CODEN: TJMEEA; ISSN: 1300-0144
PUBLISHER: Scientific and Technical Research Council of Turkey
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **120072-59-5**, SC 41930
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(leukotriene B4 receptor antagonist SC-41930 inhibition of otitis externa)
RN 120072-59-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



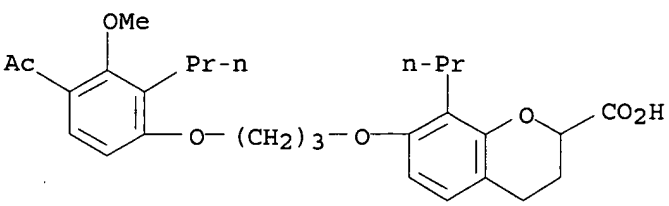
AB Sensitized guinea pigs were injected i.p. with SC-41930. One hour later, intradermal injection of killed Staphylococcus aureus into the skin of the external auditory canal was performed. Twenty-four hours after inoculation, the animals were killed, and canal skins were isolated for histopathol. evaluation. Only mild inflammatory infiltration was obsd. in the SC-41930-treated group, whereas the controls showed severe inflammatory infiltration and also deterioration of the glandular structure. Thus, SC-41930 attenuates the acute inflammatory reaction of otitis externa.

L4 ANSWER 19 OF 48 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:620228 CAPLUS
DOCUMENT NUMBER: 123:74426
TITLE: Blockade of human neutrophil activation by 2-[2-propyl-3-[3-[2-ethyl-4-(4-fluorophenyl)-5-hydroxyphenoxy]propoxy]phenoxy]benzoic acid (LY293111), a novel leukotriene B4 receptor antagonist
AUTHOR(S): Marder, Philip; Sawyer, J. Scott; Froelich, Larry L.; Mann, Larry L.; Spaethe, Stephen M.
CORPORATE SOURCE: Lilly Res. Lab., Indianapolis, IN, 46285, USA
SOURCE: Biochemical Pharmacology (1995), 49(11), 1683-90
CODEN: BCPCA6; ISSN: 0006-2952
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **120072-59-5**, SC-41930
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(blockade of human neutrophil activation by leukotriene B receptor antagonist LY293111 and comparison with SC-41930)
RN 120072-59-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



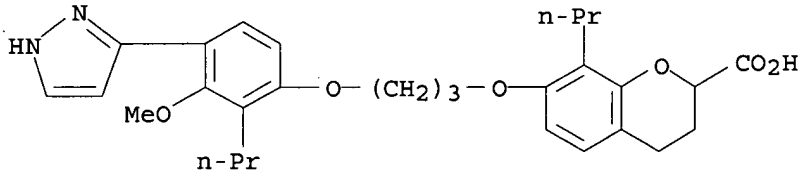
AB Leukotriene B4 (LTB4), a naturally occurring pro-inflammatory product of arachidonic acid metab., has been assocd. with human inflammatory **disease**. This study compares the abilities of two LTB4 receptor antagonists, 2-[2-propyl-3-[3-[2-ethyl-4-(4-fluorophenyl)-5-hydroxyphenoxy]-propoxy]phenoxy]benzoic acid (LY293111) and 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)-propoxy]-3,4-dihydro-8-propyl-2H-1-benzopyran-2-carboxylic acid (SC-41930), to displace LTB4 binding and their functional blockade of human neutrophil activation. LY293111 inhibited the binding of [3H]LTB4 with a Ki of 25 nM; SC-41930 displayed a similar potency (Ki = 17 nM). In contrast, LY293111 prevented LTB4-induced calcium mobilization with an IC50 = 20 nM, or 40 times more effectively than SC-41930 (IC50 = 808 nM). LY293111 was 300 times more potent than SC-41930 in blocking LTB4-induced CD11b up-regulation on isolated neutrophils. LY293111 also arrested LTB4-induced up-regulation of CD11b on neutrophils in whole human blood. LY293111 was not effective in blocking human neutrophil activation responses induced by N-formyl-methionyl-leucyl-phenylalanine (fMLP), platelet-activating factor (PAF), human recombinant endothelial interleukin-8 (IL-8) or human recombinant complement component 5a (C5a).

L4 ANSWER 20 OF 48 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:544212 CAPLUS
DOCUMENT NUMBER: 122:306099
TITLE: Antiinflammatory effects of second-generation leukotriene B4 receptor antagonist, SC-53228: impact upon leukotriene B4- and 12(R)-HETE-mediated events
AUTHOR(S): Fretland, D. J.; Anglin, C. P.; Bremer, M.; Isakson, P.; Widomski, D. L.; Paulson, S. K.; Docter, S. H.; Djuric, S. W.; Penning, T. D.; et al.
CORPORATE SOURCE: Department of Inflammatory Diseases Research, Searle Research and Development, Chesterfield, MO, USA
SOURCE: Inflammation (New York, NY, United States) (1995), 19(2), 193-205
CODEN: INFLD4; ISSN: 0360-3997
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **120072-59-5**, SC-41930
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiinflammatory effects: impact upon leukotriene B4- and 12(R)-HETE-mediated events)
RN 120072-59-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)

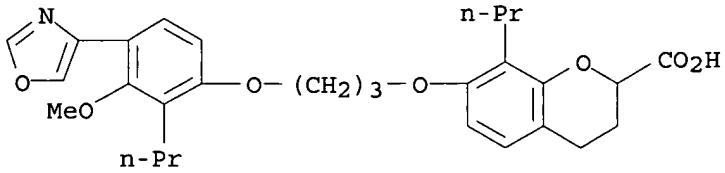


AB Leukotriene B4 (LTB4) and 12(R)-hydroxyeicosatetraenoic acid [12(R)-HETE] are proinflammatory products of arachidonic acid metab. that have been implicated as mediators in a no. of inflammatory **diseases**. When injected intradermally into the guinea pig, LTB4 and 12(R)-HETE elicit a dose-dependent migration (chemotaxis) of neutrophils (PMNs) into the injection sites as assessed by the presence of a neutrophil marker enzyme myeloperoxidase. SC-41930 {7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxyl]-3,4-dihydro-8-propyl- 2H-1-benzopyran-2-carboxylic acid}, a first-generation LTB4 receptor antagonist, inhibited the chemotactic actions of LTB4 when given orally with an ED50 value of 1.7 mg/kg. The second-generation LTB4 receptor antagonist, SC-53228 [(+)-(S)-7-(3-{2-(cyclopropylmethyl)-3-methoxy-4-[(methylamino)carbonyl]phenoxy}propoxy)-3,4-dihydro-8-propyl-2H-1-benzopyran-2-propanoic acid], inhibited LTB4-induced chemotaxis when given intragastrically with an ED50 value of 0.07 mg/kg. Furthermore, SC-53228 inhibited 12(R)-HETE-induced granulocyte chemotaxis with an oral ED50 value of 5.8 mg/kg. When dosed orally over a range of 0.03-100 mg/kg, SC-53228 gave Cmax plasma concns. of 0.015-41.1 .mu.g/mL. SC-53228 inhibited LTB4-primed membrane depolarization of human neutrophils with an IC50 value of 34 nM. As a potent LTB4 receptor antagonist, SC-53228 may well have application in the medical management of **disease** states such as asthma, rheumatoid arthritis, inflammatory bowel **disease**, contact dermatitis, and psoriasis, in which LTB4 and/or 12(R)-HETE are implicated as inflammatory mediators.

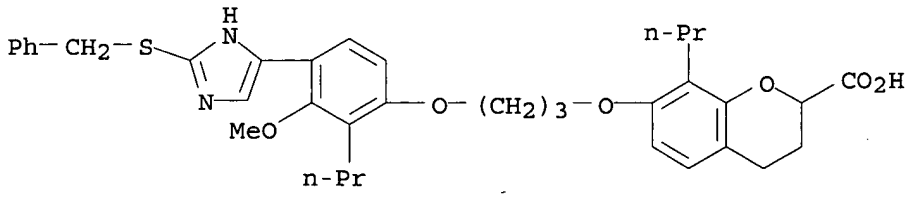
L4 ANSWER 21 OF 48 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:413307 CAPLUS
DOCUMENT NUMBER: 122:230123
TITLE: Second Generation Leukotriene B4 Receptor Antagonists Related to SC-41930: Heterocyclic Replacement of the Methyl Ketone Pharmacophore
AUTHOR(S): Penning, Thomas D.; Djuric', Stevan W.; Miyashiro, Julie M.; Yu, Stella; Snyder, James P.; Spangler, Dale; Anglin, Charles P.; Fretland, Donald J.; Kachur, James F.; et al.
CORPORATE SOURCE: Department of Chemistry, Searle Research and Development, Skokie, IL, 60077, USA
SOURCE: Journal of Medicinal Chemistry (1995), 38(6), 858-68
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **137837-12-8P 138828-24-7P 138828-27-0P**
138828-28-1P 138828-29-2P 138828-31-6P
138828-33-8P 138828-36-1P 138828-39-4P, SC 50605 **138828-42-9P 138828-44-1P 138828-46-3P**
138828-47-4P 152246-97-4P, SC 48928 **162105-82-0P**
162105-83-1P 162153-46-0P, SC 52798 **162153-47-1P**
, SC 52799
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. and structure activity relations of leukotriene B4 antagonist benzopyran carboxylic acid derivs.)
RN 137837-12-8 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 3,4-dihydro-7-[3-[3-methoxy-2-propyl-4-(1H-pyrazol-3-yl)phenoxy]propoxy]-8-propyl- (9CI) (CA INDEX NAME)



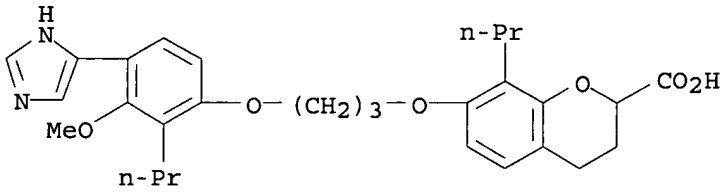
RN 138828-24-7 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 3,4-dihydro-7-[3-[3-methoxy-4-(4-oxazolyl)-2-propylphenoxy]propoxy]-8-propyl- (9CI) (CA INDEX NAME)



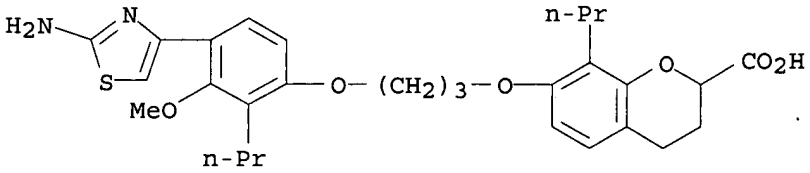
RN 138828-27-0 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 3,4-dihydro-7-[3-[3-methoxy-4-[2-[(phenylmethyl)thio]-1H-imidazol-4-yl]-2-propylphenoxy]propoxy]-8-propyl- (9CI) (CA INDEX NAME)



RN 138828-28-1 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 3,4-dihydro-7-[3-[4-(1H-imidazol-4-yl)-3-methoxy-2-propylphenoxy]propoxy]-8-propyl- (9CI) (CA INDEX NAME)

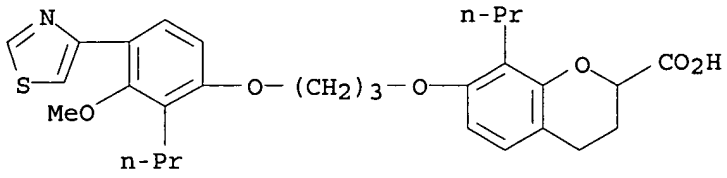


RN 138828-29-2 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[4-(2-amino-4-thiazolyl)-3-methoxy-2-propylphenoxy]propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)

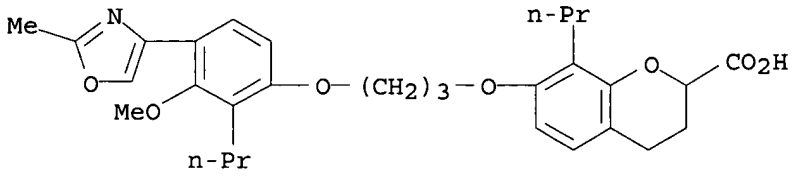


RN 138828-31-6 CAPLUS

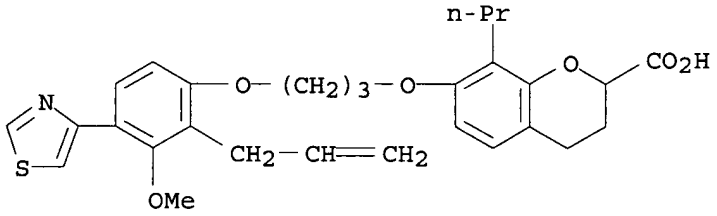
CN 2H-1-Benzopyran-2-carboxylic acid, 3,4-dihydro-7-[3-[3-methoxy-2-propyl-4-(4-thiazolyl)phenoxy]propoxy]-8-propyl- (9CI) (CA INDEX NAME)



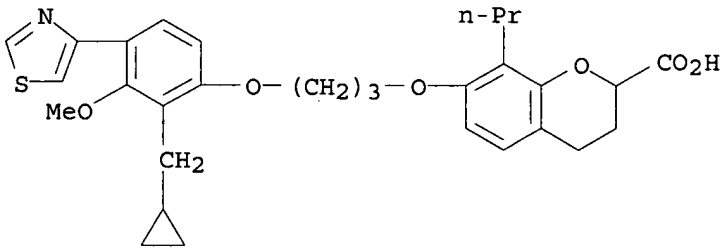
RN 138828-33-8 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 3,4-dihydro-7-[3-[3-methoxy-4-(2-methyl-4-oxazolyl)-2-propylphenoxy]propoxy]-8-propyl- (9CI) (CA INDEX NAME)



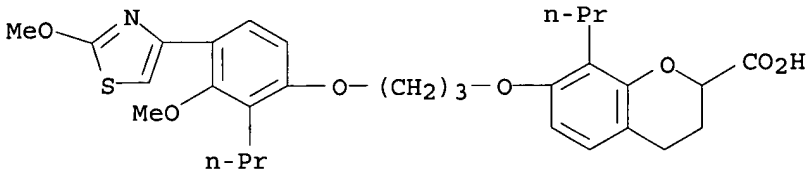
RN 138828-36-1 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 3,4-dihydro-7-[3-[3-methoxy-2-(2-propenyl)-4-(4-thiazolyl)phenoxy]propoxy]-8-propyl- (9CI) (CA INDEX NAME)



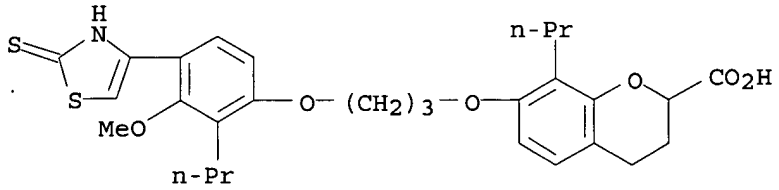
RN 138828-39-4 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[2-(cyclopropylmethyl)-3-methoxy-4-(4-thiazolyl)phenoxy]propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



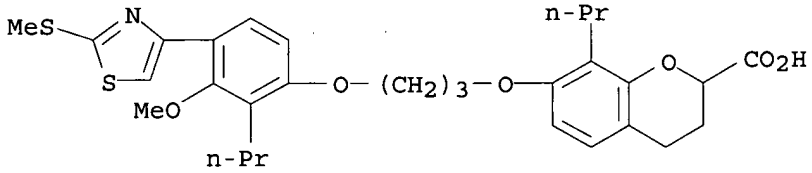
RN 138828-42-9 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 3,4-dihydro-7-[3-[3-methoxy-4-(2-methoxy-4-thiazolyl)-2-propylphenoxy]propoxy]-8-propyl- (9CI) (CA INDEX NAME)



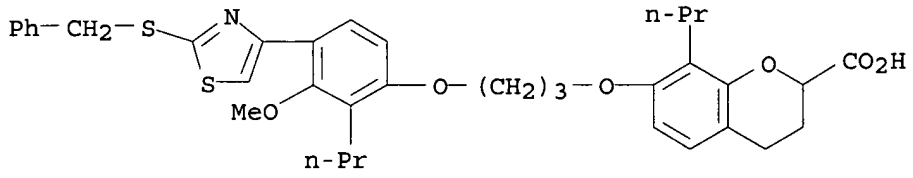
RN 138828-44-1 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[4-(2,3-dihydro-2-thioxo-4-thiazolyl)-3-methoxy-2-propylphenoxy]propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



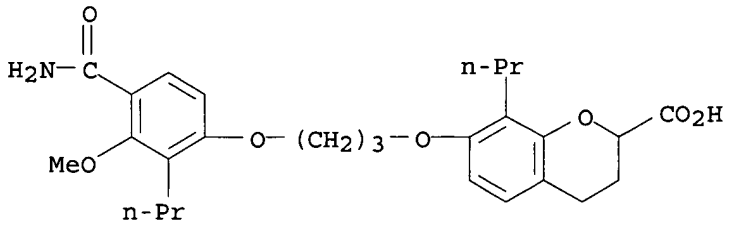
RN 138828-46-3 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 3,4-dihydro-7-[3-[3-methoxy-4-[2-(methylthio)-4-thiazolyl]-2-propylphenoxy]propoxy]-8-propyl- (9CI) (CA INDEX NAME)

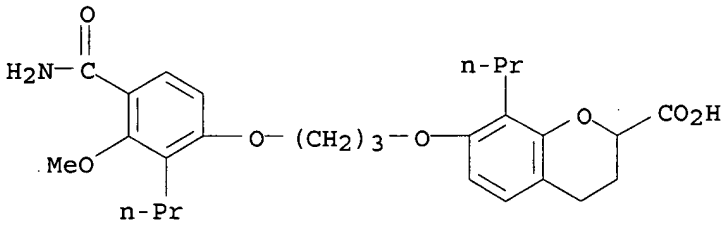


RN 138828-47-4 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 3,4-dihydro-7-[3-[3-methoxy-4-[2-[(phenylmethyl)thio]-4-thiazolyl]-2-propylphenoxy]propoxy]-8-propyl- (9CI) (CA INDEX NAME)

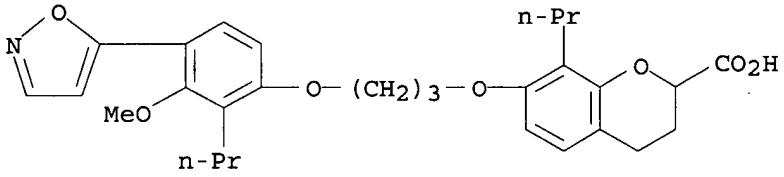


RN 152246-97-4 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[4-(aminocarbonyl)-3-methoxy-2-propylphenoxy]propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)

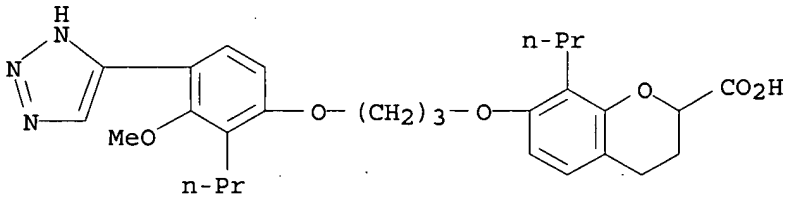




RN 162105-82-0 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 3,4-dihydro-7-[3-[4-(5-isoxazolyl)-3-methoxy-2-propylphenoxy]propoxy]-8-propyl- (9CI) (CA INDEX NAME)

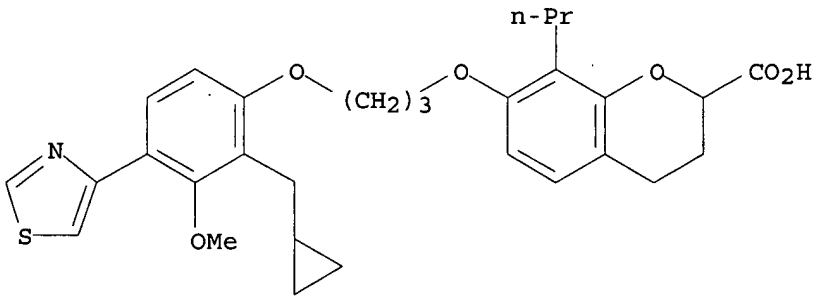


RN 162105-83-1 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 3,4-dihydro-7-[3-[3-methoxy-2-propyl-4-(1H-1,2,3-triazol-4-yl)phenoxy]propoxy]-8-propyl- (9CI) (CA INDEX NAME)



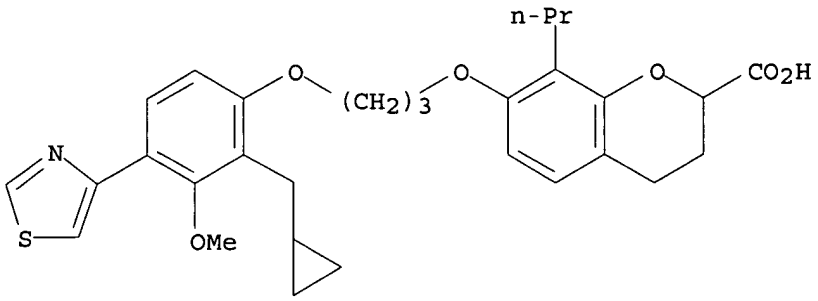
RN 162153-46-0 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[2-(cyclopropylmethyl)-3-methoxy-4-(4-thiazolyl)phenoxy]propoxy]-3,4-dihydro-8-propyl-, (+)- (9CI) (CA INDEX NAME)

Rotation (+).



RN 162153-47-1 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[2-(cyclopropylmethyl)-3-methoxy-4-(4-thiazolyl)phenoxy]propoxy]-3,4-dihydro-8-propyl-, (-)- (9CI) (CA INDEX NAME)

Rotation (-).

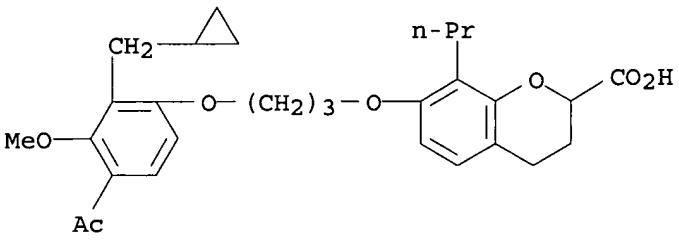


AB The previous reports have highlighted the first-generation leukotriene B4 (LTB4) receptor antagonist SC-41930 (7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl-2H-1-benzopyran-2-carboxylic acid) which has potent oral, topical, and intracolonic activity in various animal models of inflammation. Extensive structure-activity relation studies, in which a series of heterocyclic replacements for the Me ketone functional group of SC-41930 was explored, identified SC-50605 (7-[3-[2-(cyclopropylmethyl)-3-methoxy-4-(4-thiazolyl)phenoxy]propoxy]-3,4-dihydro-8-propyl-2H-1-benzopyran-2-carboxylic acid) as an optimized analog within a series of thiazoles. SC-50605 was significantly more potent than SC-41930 in LTB4 receptor binding, chemotaxis, and degranulation assays. It also displayed very good activity in animal models of colitis and epidermal inflammation by oral, topical, i.v., and intracolonic routes of administration. The resolved enantiomers of SC-50605 were obtained by chiral chromatog. and both demonstrated good in vitro and in vivo activity. The (+)-isomer (SC-52798) is currently being evaluated as a potential clin. candidate for psoriasis and ulcerative colitis therapy.

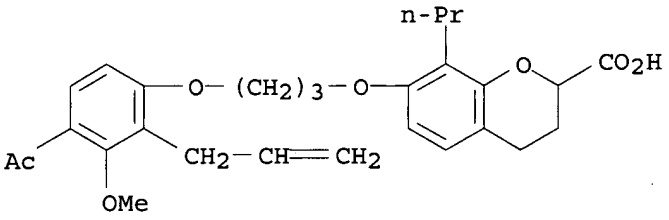
L4 ANSWER 22 OF 48 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:354656 CAPLUS
DOCUMENT NUMBER: 122:187398
TITLE: Anti-inflammatory benzopyrans, compositions and method of their use
INVENTOR(S): Djuric, Stevan W.; Fretland, Donald J.; Yu, Stella S.
PATENT ASSIGNEE(S): G. D. Searle and Co., USA
SOURCE: U.S., 12 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5380740	A	19950110	US 1993-50109	19930428

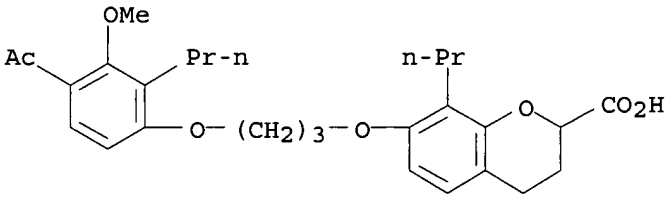
OTHER SOURCE(S): MARPAT 122:187398
IT **120072-38-0 120072-40-4 120072-59-5**
RL: RCT (Reactant); RACT (Reactant or reagent)
(benzopyran derivs. as LTB4 antagonists and antiinflammatory agents)
RN 120072-38-0 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[4-acetyl-2-(cyclopropylmethyl)-3-methoxyphenoxy]propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



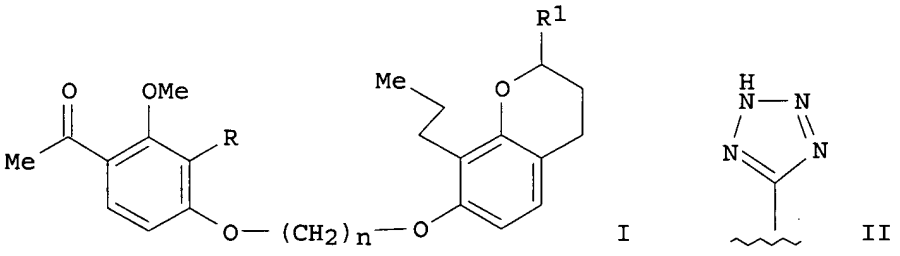
RN 120072-40-4 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[4-acetyl-3-methoxy-2-(2-propenyl)phenoxy]propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



RN 120072-59-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



GI



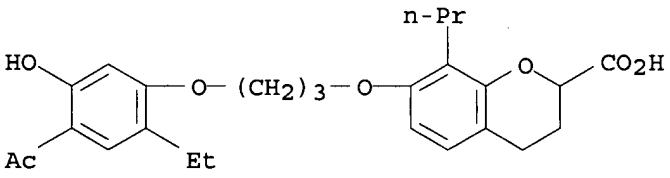
AB This invention encompasses compds. of the formula I [wherein R represents lower alkyl of 1 to 6 carbon atoms, lower alkenyl of 2 to 6 carbon atoms, or (CH2)mR3 wherein R3 represents cycloalkyl of 3 to 5 carbon atoms and m is 1, 2 or 3; R1 is CONH2 or CONHSO2R2 wherein R2 is lower alkyl, Ph, unsubstituted or substituted with lower alkyl, or II; and n is an integer from 2 to 5] and the stereoisomers and pharmaceutically acceptable salts thereof. The compds. are useful anti-inflammatory agents for treating, for example, inflammatory bowel **disease**, rheumatoid arthritis, gout, asthma and psoriasis. LTB4 receptor binding relative to 7-[3,(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl-2H-

1-benzopyran-2-carboxylic acid: 0.8-2.0 vs. 1 (where IC50 for the ref. compd. = 3 .times. 10-7 M). Pharmaceutical formulations were given.

L4 ANSWER 23 OF 48 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:541719 CAPLUS
DOCUMENT NUMBER: 121:141719
TITLE: Leukotriene B4 antagonists
INVENTOR(S): Dillard, Robert D.; Sawyer, J. Scott; Sofia, Michael J.
PATENT ASSIGNEE(S): Lilly, Eli, and Co., USA
SOURCE: U.S., 33 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

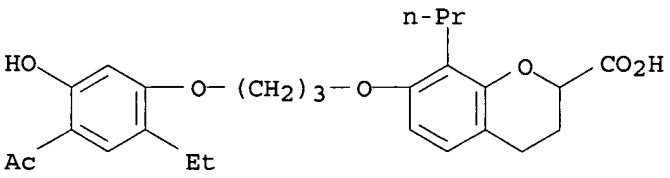
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5324743	A	19940628	US 1992-988615	19921210
US 5552441	A	19960903	US 1994-195951	19940214

PRIORITY APPLN. INFO.: US 1992-988615 19921210
OTHER SOURCE(S): MARPAT 121:141719
IT **155453-11-5P 156005-50-4P 157230-27-8P**
RL: PREP (Preparation)
(prepn. and leukotriene B4 antagonist activity of)
RN 155453-11-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-2-ethyl-5-hydroxyphenoxy)propoxy]-3,4-dihydro-8-propyl-, monosodium salt (9CI) (CA INDEX NAME)

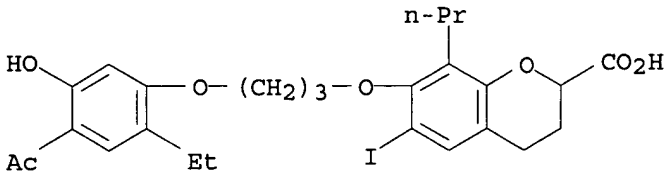


● Na

RN 156005-50-4 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-2-ethyl-5-hydroxyphenoxy)propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



RN 157230-27-8 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-2-ethyl-5-hydroxyphenoxy)propoxy]-3,4-dihydro-6-iodo-8-propyl- (9CI) (CA INDEX NAME)



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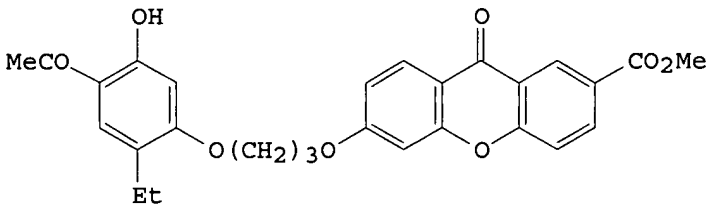


I

AB This invention provides certain 1,2,4,5 substituted benzene derivs. contg. "acid" substituents derived from cyclic or hetercyclic moieties. These unique compds. are leukotriene B4 antagonists and formulation of these derivs., and a method of using these derivs. for the treatment of **conditions** characterized by an excessive release of leukotrienes. E.g., I was prepd. and incorporated into hard gelatin capsules. The leukotriene B4 antagonist activity of a no. of compds. was demonstrated.

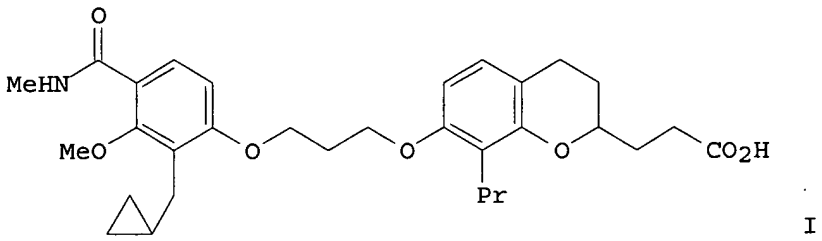
L4 ANSWER 24 OF 48 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:533968 CAPLUS
DOCUMENT NUMBER: 121:133968
TITLE: (Phenoxypropoxy)benzopyranpropanoates as (phenoxypropoxy)benzopyranpropanoatesleukotriene B4 antagonists
INVENTOR(S): Djuric, Stevan W.; Docter, Stephen H.; Yu, Stella S.
PATENT ASSIGNEE(S): Searle, G. D., and Co., USA
SOURCE: U.S., 27 pp. Cont.-in-part of U.S. 5,124,350. CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5310951	A	19940510	US 1992-995859	19921223
US 5124350	A	19920623	US 1990-545430	19900628
AT 131165	E	19951215	AT 1991-916271	19910627
ES 2080334	T3	19960201	ES 1991-916271	19910627
US 5439937	A	19950808	US 1994-205909	19940303
US 5532383	A	19960702	US 1995-445059	19950519

PRIORITY APPLN. INFO.: US 1990-545430 19900628
US 1992-995859 19921223
US 1994-205909 19940303

IT **157062-25-4P 157062-38-9P 157062-41-4P**
157062-43-6P 157062-46-9P 157062-48-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as leukotriene antagonist)
RN 157062-25-4 CAPLUS
RN 157062-38-9 CAPLUS
RN 157062-41-4 CAPLUS

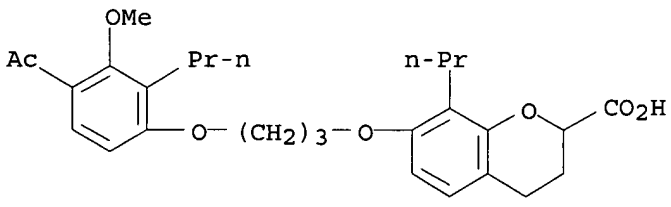
RN 157062-43-6 CAPLUS
RN 157062-46-9 CAPLUS
RN 157062-48-1 CAPLUS
GI



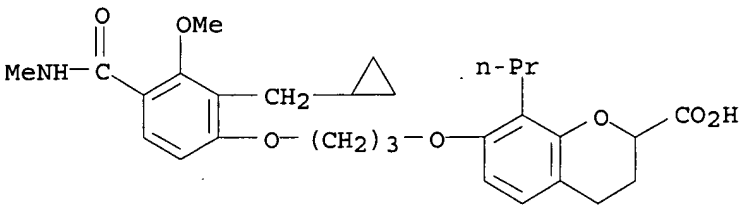
I

AB Two compds., 7-[3-[2-(cyclopropylmethyl)-3-methoxy-4-[(methylamino)carbonyl]phenoxy]propoxy]-3,4-dihydro-8-propyl-H-1-benzopyran-2-propanoic acid, (+)-I and (-)-I, are claimed. I are leukotriene B4 antagonists and are useful as antiinflammatory agents and in treating **disease conditions** mediated by LTB4.

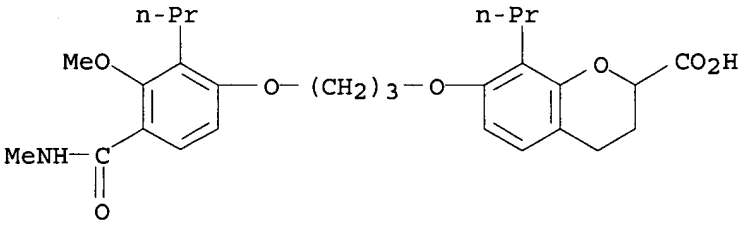
L4 ANSWER 25 OF 48 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:435262 CAPLUS
DOCUMENT NUMBER: 121:35262
TITLE: Synthesis and pharmacological activity of SC-53228, a leukotriene B4 receptor antagonist with high intrinsic potency and selectivity
AUTHOR(S): Djuric, Stevan W.; Docter, Stephen H.; Yu, Stella S.; Spangler, Dale; Tsai, Bie Shung; Anglin, Charles P.; Gaginella, Timothy S.; Kachur, James F.; Keith, Robert H.; et al.
CORPORATE SOURCE: Searle R and D, Skokie, IL, 60077, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (1994), 4(6), 811-16
CODEN: BMCLE8; ISSN: 0960-894X
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **120072-59-5**, SC-41930 **141059-14-5** **141059-28-1** **152246-97-4**, SC 48928 **155878-64-1** **155878-65-2** **155878-66-3**
RL: RCT (Reactant); RACT (Reactant or reagent)
(leukotriene antagonist activity of)
RN 120072-59-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



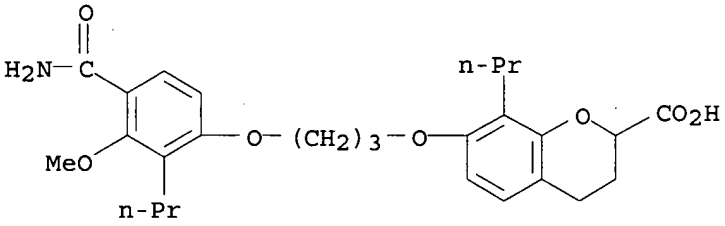
RN 141059-14-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[2-(cyclopropylmethyl)-3-methoxy-4-[(methylamino)carbonyl]phenoxy]propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



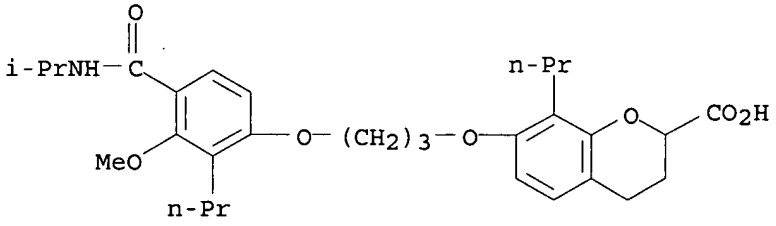
RN 141059-28-1 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 3,4-dihydro-7-[3-[3-methoxy-4-[(methylamino)carbonyl]-2-propylphenoxy]propoxy]-8-propyl- (9CI) (CA INDEX NAME)



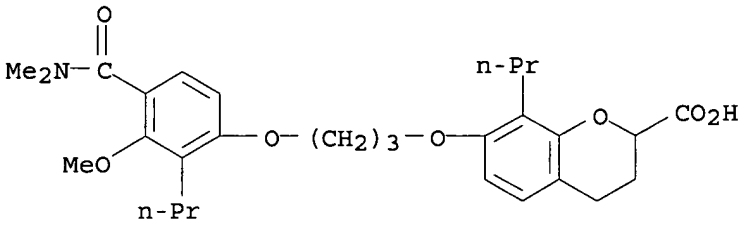
RN 152246-97-4 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[4-(aminocarbonyl)-3-methoxy-2-propylphenoxy]propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



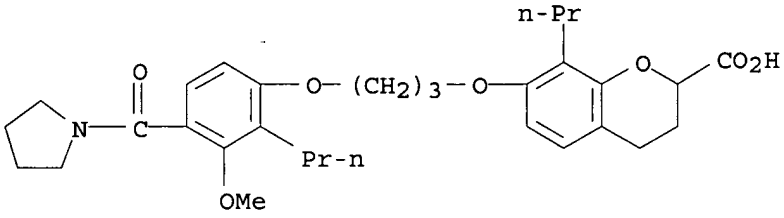
RN 155878-64-1 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 3,4-dihydro-7-[3-[3-methoxy-4-[[(1-methylethyl)amino]carbonyl]-2-propylphenoxy]propoxy]-8-propyl- (9CI) (CA INDEX NAME)



RN 155878-65-2 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[4-[(dimethylamino)carbonyl]-3-methoxy-2-propylphenoxy]propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



RN 155878-66-3 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 3,4-dihydro-7-[3-[3-methoxy-2-propyl-4-(1-pyrrolidinylcarbonyl)phenoxy]propoxy]-8-propyl- (9CI) (CA INDEX NAME)



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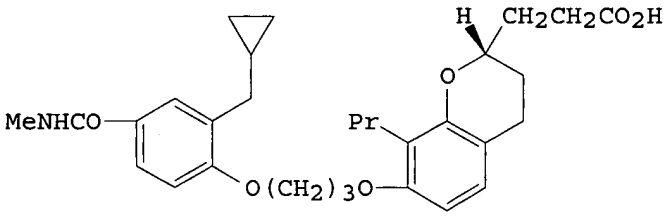
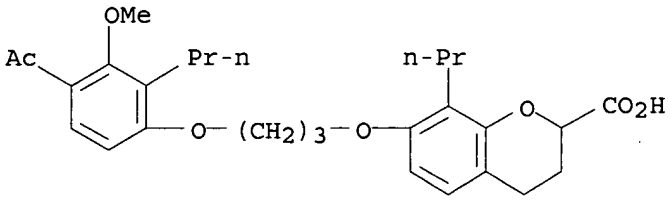


I

AB The structure activity relationship (SAR) studies leading to the identification of a novel high potency Leukotriene B4 receptor antagonist SC-53228 (I) are delineated. This compd. shows excellent pharmacodynamic efficacy in animal models of inflammatory **disease**.

L4 ANSWER 26 OF 48 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:95122 CAPLUS
DOCUMENT NUMBER: 120:95122
TITLE: Ocular antiinflammatory activity of SC-41930, a specific leukotriene B4 receptor antagonist
AUTHOR(S): Kaya, Murat; Energin, Fethi; Mensiz, Ercan; Erim, Adnan; Resi, Abdulkadir; Arseven, Gursel
CORPORATE SOURCE: Med. Fac., Ataturk Univ., Erzurum, Turk.
SOURCE: Turkish Journal of Medical Sciences (1993), 18(4), 295-301
CODEN: TJMEEA; ISSN: 1300-0144
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **120072-59-5**, SC-41930
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiinflammatory activity of, in eye, leukotriene B4 receptor antagonism in relation to)
RN 120072-59-5 CAPLUS

CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



AB Endogenous ocular inflammations are still major problems in ophthalmol. Recently attention was focussed on the 5-lipoxygenase product leukotriene B4 (LTB4) which is thought to be a prominent proinflammatory mediator in acute inflammatory reactions. The authors evaluated the antiinflammatory efficacy of the leukotriene B4 receptor antagonist SC-41930 on ocular inflammation in rabbits. Animals were challenged in the anterior chamber 2 wk after a s.c. injection of staphylococcus antigens dissolved in Freund's Complete Adjuvant. In the exptl. group, IV administration of SC-41930 was given 30 min before and after anterior chamber challenge, while in the control group, sodium bicarbonate was given in the same manner. Twenty-four hours after the ocular challenge, slit lamp examn. was performed to look for signs of anterior chamber inflammation; then the animals were sacrificed, the eyes were enucleated and histopathol. examn. was performed. Chi-square test was used in statistical analyses for results of scores in slit-lamp examns. In SC-41930-treated eyes, there was a mild acute inflammatory infiltration in anterior chambers while in control groups that received only sodium bicarbonate, a moderate to marked acute inflammatory infiltration was obsd. in anterior chambers. It seems that the drug is likely to have a potential use in ophthalmol. as an antiinflammatory agent.

L4 ANSWER 27 OF 48 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:45965 CAPLUS
DOCUMENT NUMBER: 120:45965
TITLE: Methods of treating aphthous ulcers and other mucocutaneous **disorders**
INVENTOR(S): Vora, Kakubhai R.; Khandwala, Atul; Smith, Charles G.
PATENT ASSIGNEE(S): Chemex/Block Drug, JV, USA
SOURCE: Can. Pat. Appl., 26 pp.
CODEN: CPXXEB
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

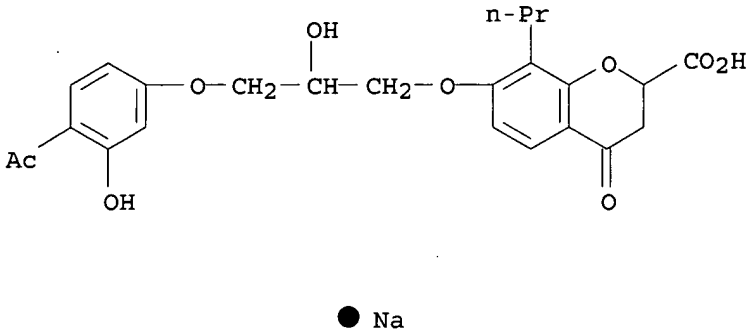
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CA 2065496	AA	19921010	CA 1992-2065496	19920409
JP 05097706	A2	19930420	JP 1992-87185	19920408
EP 518798	A2	19921216	EP 1992-470014	19920409
EP 518798	A3	19941207		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, PT, SE				
EP 836852	A1	19980422	EP 1997-202524	19920409
EP 836852	B1	20011017		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT				
AT 206922	E	20011115	AT 1997-202524	19920409
ES 2166043	T3	20020401	ES 1997-202524	19920409

PRIORITY APPLN. INFO.: US 1991-682347 A 19910409
EP 1992-470014 A3 19920409
OTHER SOURCE(S): MARPAT 120:45965
IT **149930-67-6**

RL: BIOL (Biological study)
(compn. contg., for treating aphthous ulcers and mucocutaneous **disorders**)

RN 149930-67-6 CAPLUS

CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-3-hydroxyphenoxy)-2-hydroxypropoxy]-3,4-dihydro-4-oxo-8-propyl-, monosodium salt (9CI) (CA INDEX NAME)



AB For treatment of aphthous ulcers and mucocutaneous **disorders**, a compn. contg. .gtoreq.1 drug selected from mediator release inhibitors; 5-lipoxygenase inhibitors; leukotriene antagonists; and platelet-activating factor antagonists is claimed. Patients with aphthous ulcers treated twice a day for three days with 5% treating agent showed clin. significant improvement in all parameters (e.g. ulcer size and redn. in erythema) measured over the vehicle paste.

L4 ANSWER 28 OF 48 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1994:274 CAPLUS

DOCUMENT NUMBER: 120:274

TITLE: Anti-colitic efficacy of SC-41930 in colitic cotton-top tamarins

AUTHOR(S): Clapp, N.; Henke, M.; Hansard, R.; Carson, R.; Fretland, D.

CORPORATE SOURCE: Marmoset Res. Cent., Oak Ridge Assoc. Univ., Oak Ridge, TN, USA

SOURCE: Agents and Actions (1993), 39(Spec. Conf. Issue), C36-C38
CODEN: AGACBH; ISSN: 0065-4299

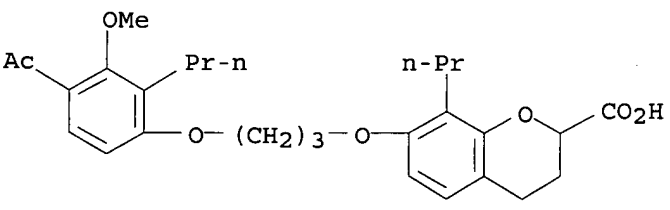
DOCUMENT TYPE: Journal

LANGUAGE: English

IT **120072-59-5**, SC-41930
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(anticolitic activity of, as leukotriene B4 antagonist in cotton-top tamarin)

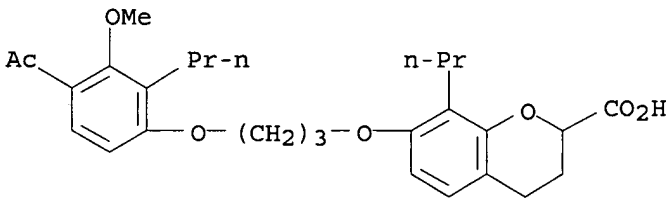
RN 120072-59-5 CAPLUS

CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



AB To evaluate anti-colitic efficacy, eight cotton-top tamarins (CTTs) with histol. confirmed persistent active colitis were given the anti-inflammatory agent SC-41930 (10 mg/kg BW by gavage BID) for eight weeks. Colonic endoscopy and biopsy observations, CBCs and clin. chemistries, and stool consistency were evaluated pre-, mid-, and posttreatment. Colitic activity was graded histol. from A1 (mild) to A5 (severe); results varied among the seven animals that completed the study; five improved, one worsened, and one was unchanged. Serum enzyme levels were significantly reduced with treatment. Stool **condition** remained puddly throughout treatment and body wts. did not vary from pretreatment levels. However, SC-41930 produced histol. evidence (reduced nos. of polymorphonuclear cells) of anti-colitic efficacy over an eight-week treatment period in CTTs with persistent active colitis. These results support the use of the CTT colitis model to evaluate efficacy of therapeutic agents and provide useful predictive information to aid in the medical management of human IBD.

L4 ANSWER 29 OF 48 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:271 CAPLUS
DOCUMENT NUMBER: 120:271
TITLE: Inflammatory mediator changes in cotton-top tamarins (CTT) after SC-41930 anti-colitic therapy
AUTHOR(S): Clapp, N.; Henke, M.; Hansard, R.; Carson, R.; Walsh, R.; Widomski, D.; Anglin, C.; Fretland, D.
CORPORATE SOURCE: Marmoset Res. Cent., Oak Ridge Assoc. Univ., Oak Ridge, TN, USA
SOURCE: Agents and Actions (1993), 39(Spec. Conf. Issue), C8-C10
CODEN: AGACBH; ISSN: 0065-4299
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **120072-59-5**, SC-41930
RL: BIOL (Biological study)
(colitis treatment by, modulation of inflammatory mediators in)
RN 120072-59-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)

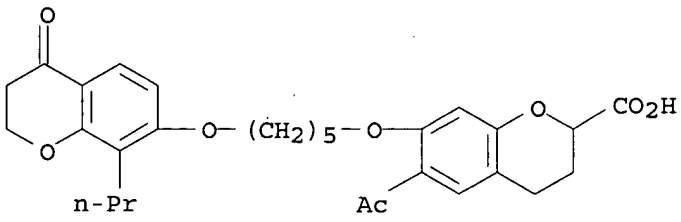


AB Use of the CTT model provides insight into the inflammatory mediator contribution in the pathogenesis of idiopathic colitis. To evaluate anti-colitic efficacy, the leukotriene B4 receptor antagonist and anti-inflammatory agent, SC-41930, was administered (10 mg/kg BW by gavage BID) for 8 wk to CTTs with histol. confirmed persistent and defined active colitis. The inflammatory mediators LTB4, PGE2, TXB2, and PAF were assayed in colonic dialyzate that was collected after 1 1/2 h from four CTTs pre-, mid-, and post-treatment, frozen at -70.degree.C, and analyzed by RIA after HPLC purifn. LTB4 levels were lower at mid- and post-treatment and had little inter-animal variation post-treatment. PGE2 and PAF levels were elevated during SC-41930 treatment, but there was a trend towards lower thromboxane B2 levels. Reduced LTB4 (PMN degranulation and chemotaxis) and increased PGE2 (mucosal-protective effect), may, in part, explain the obsd. efficacy of SC-41930 in active tamarin colitis.

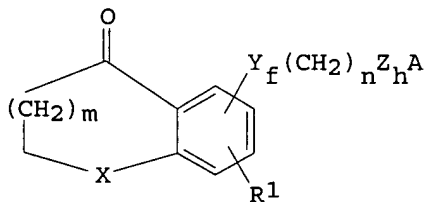
L4 ANSWER 30 OF 48 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:625820 CAPLUS
DOCUMENT NUMBER: 119:225820
TITLE: Preparation of benzopyranonecarboxylic acid derivatives as antiinflammatants
INVENTOR(S): Cohen, Noal; Lee, Ferdinand Kwo Chen; Yagaloff, Keith Alan
PATENT ASSIGNEE(S): Hoffmann-La Roche, F., und Co. A.-G., Switz.
SOURCE: Eur. Pat. Appl., 128 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 531823	A1	19930317	EP 1992-114691	19920828
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
US 5273999	A	19931228	US 1992-898852	19920615
RU 2067973	C1	19961020	RU 1992-5052388	19920828
CA 2077213	AA	19930311	CA 1992-2077213	19920831
HU 66238	A2	19941028	HU 1992-2817	19920902
ZA 9206691	A	19930310	ZA 1992-6691	19920903
AU 9222191	A1	19930311	AU 1992-22191	19920907
AU 655057	B2	19941201		
NO 9203508	A	19930311	NO 1992-3508	19920909
CN 1071423	A	19930428	CN 1992-111386	19920909
JP 05201915	A2	19930810	JP 1992-266694	19920909
BR 9203508	A	19930413	BR 1992-3508	19920910
US 5434186	A	19950718	US 1993-128612	19930928

PRIORITY APPLN. INFO.: US 1991-757100 19910910
US 1992-898852 19920615
OTHER SOURCE(S): MARPAT 119:225820
IT **150597-26-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as LTB4 antagonist)
RN 150597-26-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 6-acetyl-7-[[5-[(3,4-dihydro-4-oxo-8-propyl-2H-1-benzopyran-7-yl)oxy]pentyl]oxy]-3,4-dihydro- (9CI) (CA INDEX NAME)



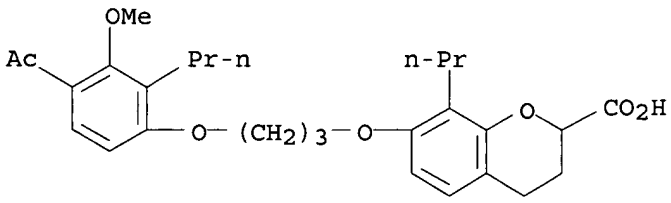
GI



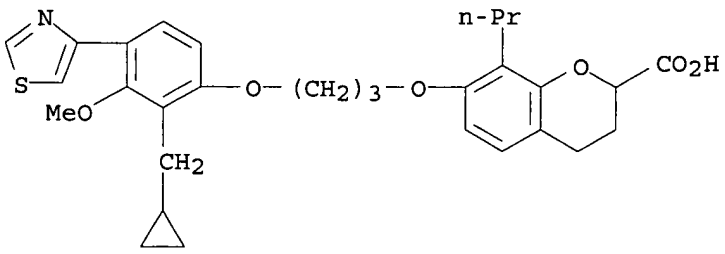
I

AB Title compds. [I; X = O, CH2; Y = O, CH2CH2, CH:CH, C.tplbond.C, OCH2C6H4; Z = CH2CH2, CH:CH, C.tplbond.C; R1 = H, alkyl, alkenyl, cycloalkyl, aralkyl; A = B, OB; B = substituted mono-, bi-, or tricyclic (hetero)aryl; h, m = 0, 1; n = 1-12], were prepd. as LTB4 antagonists. Thus, 2,3-dihydro-7-hydroxy-8-propyl-4H-1-benzopyran-4-one (prepn. given) was alkylated with Me 2-[(6-methoxy-6-oxohexyl)oxy]-6-[6-(methylsulfonyl)oxyhexyl]benzenepropanoate (prepn. given) followed by sapon. to give 2-[(5-carboxypentyl)oxy]-6-[6-[(3,4-dihydro-4-oxo-8-propyl-2H-1-benzopyran-7-yl)oxy]hexyl]benzenepropanoic acid (II). II inhibited LTB4-induced bronchoconstriction with ID50 = 0.07 mg/kg i.v. Dosage forms were prepd. contg. II.

L4 ANSWER 31 OF 48 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:595290 CAPLUS
DOCUMENT NUMBER: 119:195290
TITLE: Leukotriene B4-induced granulocyte trafficking in guinea pig dermis: effect of second-generation leukotriene B4 receptor antagonists, SC-50605 and SC-51146
AUTHOR(S): Fretland, D. J.; Widomski, D. L.; Anglin, C. P.; Penning, T. D.; Yu, S.; Djuric, S. W.
CORPORATE SOURCE: Dep. Immunoinflammat. Dis. Res., Skokie, IL, 60077, USA
SOURCE: Inflammation (New York, NY, United States) (1993), 17(3), 353-60
CODEN: INFLD4; ISSN: 0360-3997
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **120072-59-5**, SC-41930 **138828-39-4**, SC 50605
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiinflammatory activity of, as leukotriene B4 receptor antagonist, neutrophil chemotaxis inhibition by)
RN 120072-59-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)

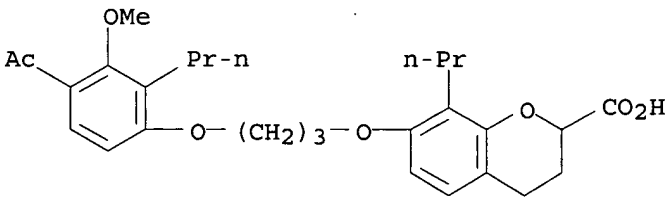


RN 138828-39-4 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[2-(cyclopropylmethyl)-3-methoxy-4-(4-thiazolyl)phenoxy]propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



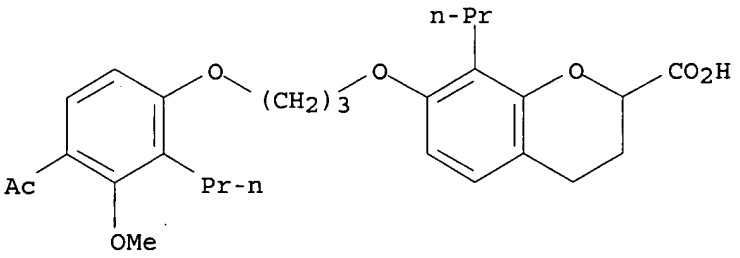
AB Leukotriene B4 (LTB4) is a proinflammatory product of arachidonic acid metab. that has been implicated as a mediator in a no. of inflammatory **diseases**. When injected intradermally into the guinea pig, LTB4 elicits a dose-dependent migration (chemotaxis) of neutrophils (PMNs) into the injection sites as assessed by the presence of a neutrophil marker enzyme myeloperoxidase. SC-41930 {7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl-2H-1-benzopyran-2-carboxylic acid}, a first-generation LTB4 receptor antagonist inhibited the chemotactic actions of LTB4 when coadministered into the dermal site and when given orally with ED50 values of 340 ng and 1.7 mg/kg, resp. The second-generation LTB4 receptor antagonists SC-50605 {7-[3-2(cyclopropylmethyl)-3-methoxy-4-(4-thiazolyl)phenoxy]propoxy]-3,4-dihydro-8-propyl-2H-1-benzopyran-2-carboxylic acid} and SC-51146 {7-[3-[2(cyclopropylmethyl)-3-methoxy-4-[(methylamino)carbonyl]phenoxy]propoxy]-3,4-dihydro-8-propyl-2H-1-benzopyran-2-propanoic acid} inhibited LTB4-induced chemotaxis when coadministered with ED50 values of 70 ng and 32 ng, resp., and when given intragastrically with ED50 values of 0.10 and 0.09 mg/kg, resp. SC-41930, SC-50605, and SC-51146 had oral durations of action of 5.5, 15, and 21 h, resp. These potent, LTB4 receptor antagonists may well have application in the medical management of **disease** states such as asthma, rheumatoid arthritis, inflammatory bowel **disease**, contact dermatitis, and psoriasis, where LTB4 is implicated as an inflammatory mediator.

L4 ANSWER 32 OF 48 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:73307 CAPLUS
DOCUMENT NUMBER: 118:73307
TITLE: Optical isomers of a leukotriene B4 antagonist have differential effects on granulocyte diapedesis in the guinea pig dermis
AUTHOR(S): Fretland, Donald J.; Widomski, Deborah L.; Anglin, Charles P.; Yu, Stella; Djuric, Stevan W.
CORPORATE SOURCE: Dep. Immunoinflammatory Dis. Res., Searle Res. and Dev., Skokie, IL, 60077, USA
SOURCE: Chirality (1992), 4(6), 353-5
CODEN: CHRLEP; ISSN: 0899-0042
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **120072-59-5**, SC-41930 **145707-13-7**, (+)SC-41930
145707-14-8, (-)SC-41930
RL: BIOL (Biological study)
(granulocyte diapedesis inhibition by, in dermis)
RN 120072-59-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



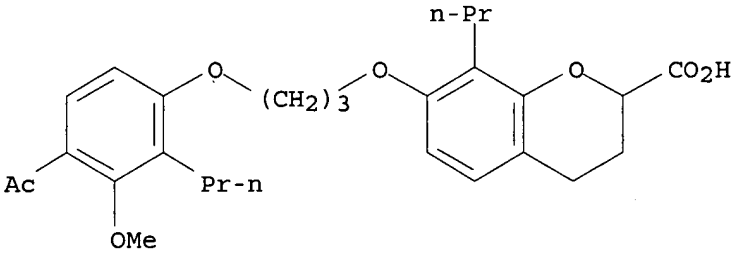
RN 145707-13-7 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl-, (+)- (9CI) (CA INDEX NAME)

Rotation (+).



RN 145707-14-8 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl-, (-)- (9CI) (CA INDEX NAME)

Rotation (-).



AB Leukotriene B4 (LTB4) is a proinflammatory product of arachidonic acid metab. that has been implicated in a no. of inflammatory **diseases**. When injected intradermally into the guinea pig, LTB4 has been shown to elicit a dose-dependent infiltration of granulocytes as assessed by the level of the neutrophil marker enzyme myeloperoxidase. SC-41930 [7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl-2H-1-benzopyran-2-carboxylic acid] is a potent LTB4 receptor antagonist. When compds. were coadministered along with LTB4 (35 ng) into the dermal site, racemic SC-41930, (+)-SC-41930, and (-)-SC-41930 each inhibited granulocyte accumulation with ED50 values of 340 .+-. 30, 98 .+-. 5.7, and 1000 .+-. 142 ng, resp.; when given i.v. inhibited with ED50 values of 0.5 .+-. 0.06, 0.3 .+-. 0.04, and 1.4 .+-. 0.19 mg/kg, resp.; and when given intragastrically inhibited with ED50 values of 1.7 .+-. 0.20, 1.4 .+-. 0.23, and 3.0 .+-. 0.41 mg/kg, resp.

L4 ANSWER 33 OF 48 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:414418 CAPLUS
DOCUMENT NUMBER: 117:14418
TITLE: Antiallergic compositions containing platelet-activating factor antagonists and leukotriene D4 antagonists
INVENTOR(S): O'Donnell, Margaret; Welton, Ann
PATENT ASSIGNEE(S): Hoffmann-La Roche, F., A.-G., Switz.
SOURCE: Eur. Pat. Appl., 16 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 469477	A1	19920205	EP 1991-112577	19910726
EP 469477	B1	19950920		
R: AT, BE, CH, DE, DK, FR, GB, IT, LI, LU, NL, SE				
AT 128030	E	19951015	AT 1991-112577	19910726

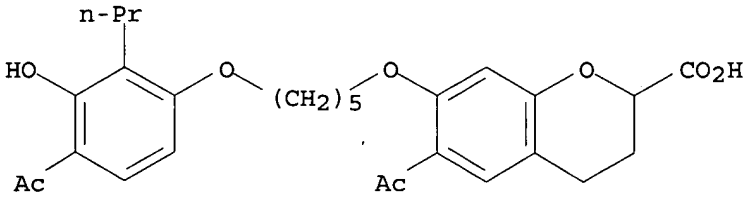
CA 2048236	AA	19920203	CA 1991-2048236	19910731
ZA 9106036	A	19920527	ZA 1991-6036	19910731
AU 9181535	A1	19920213	AU 1991-81535	19910801
AU 651358	B2	19940721		
JP 04244028	A2	19920901	JP 1991-216009	19910801
US 5227378	A	19930713	US 1992-848564	19920309

PRIORITY APPLN. INFO.: US 1990-561743 19900802

IT **96566-25-5D**, mixts. with platelet-activating factor antagonists **140667-06-7**
RL: BIOL (Biological study)
(antiallergic compns. contg.)

RN 96566-25-5 CAPLUS

CN 2H-1-Benzopyran-2-carboxylic acid, 6-acetyl-7-[[5-(4-acetyl-3-hydroxy-2-propylphenoxy)pentyl]oxy]-3,4-dihydro- (9CI) (CA INDEX NAME)

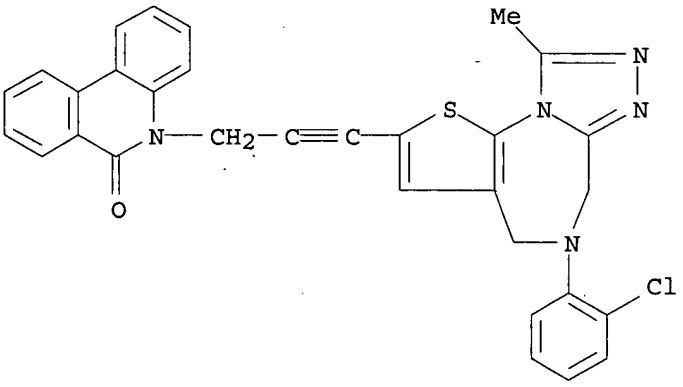


RN 140667-06-7 CAPLUS

CN 2H-1-Benzopyran-2-carboxylic acid, 6-acetyl-7-[[5-(4-acetyl-3-hydroxy-2-propylphenoxy)pentyl]oxy]-3,4-dihydro-, mixt. with 5-[3-[5-(2-chlorophenyl)-5,6-dihydro-9-methyl-4H-thieno[3,2-f][1,2,4]triazolo[4,3-a][1,4]diazepin-2-yl]-2-propynyl]-6(5H)-phenanthridinone (9CI) (CA INDEX NAME)

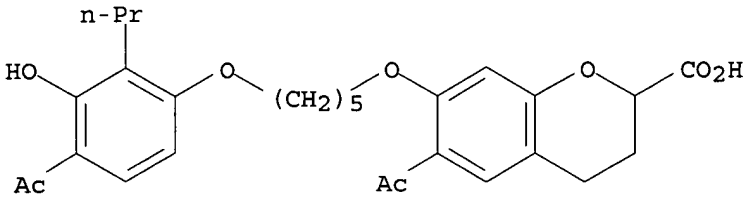
CM 1

CRN 140634-85-1
CMF C31 H22 Cl N5 O S



CM 2

CRN 96566-25-5
CMF C28 H34 O8

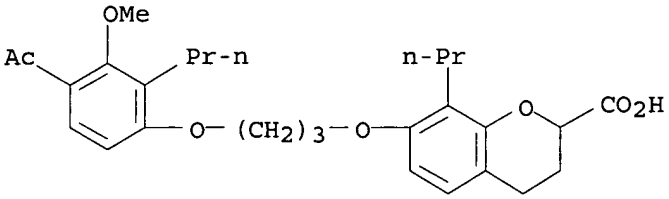


AB A synergistic combination of platelet activating factor (PAF) antagonists with leukotriene D4 (LTD4) antagonists provides protection against allergic reactions, such as antigen-induced death. Guinea pigs were sensitized with an i.p. injection of ovalbumin in a saline soln. and administered with a combination of 5-[3-[4-(2-chlorophenyl)-9-methyl-6H-thieno[3,2-f]1,2,4]triazolo[4,3-a][1,4]diazepin-2-yl]-2-propynyl]phenanthridin-6(5H)-one (I) (PAF antagonist) and (E)-4-[3-[2-(4-cyclobutyl-2-thiazolyl)ethenyl]phenylamino]-2,2-diethyl-4-oxobutanoic acid (II) (LTD4 antagonist) at 1 mg/kg each before challenge with antigen; a survival rate from anaphylactic death at 120 min was 100 %, compared to 0 % for groups administered with I or II alone. Formulations contg. I and II combinations are given.

L4 ANSWER 34 OF 48 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:214350 CAPLUS
DOCUMENT NUMBER: 116:214350
TITLE: Preparation of 3,4-dihydro-7-[(carbamoylphenoxy)alkoxy]benzopyran-2-alkanoates and analogs as LTB4 antagonists
INVENTOR(S): Djuric, Stevan Wakefield; Docter, Stephen Hermann; Yu, Stella Siu Tzyy
PATENT ASSIGNEE(S): Searle, G. D., and Co., USA
SOURCE: PCT Int. Appl., 149 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9200011	A2	19920109	WO 1991-US4386	19910627
WO 9200011	A3	19920206		
W: AT, AU, BB, BG, BR, CA, CH, CS, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MC, MG, NL, NO, PL				
RW: AT, BE, BF, BJ, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GN, GR, IT, LU, NL, SE, SN, TD, TG				
US 5124350	A	19920623	US 1990-545430	19900628
AU 9185282	A1	19920123	AU 1991-85282	19910627
JP 05507720	T2	19931104	JP 1991-515594	19910627
JP 2942630	B2	19990830		
EP 593478	A1	19940427	EP 1991-916271	19910627
EP 593478	B1	19951206		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
AT 131165	E	19951215	AT 1991-916271	19910627
ES 2080334	T3	19960201	ES 1991-916271	19910627

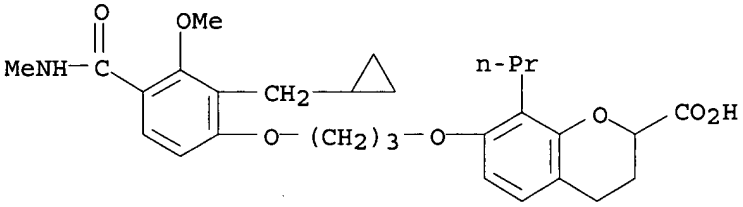
PRIORITY APPLN. INFO.: US 1990-545430 19900628
WO 1991-US4386 19910627
OTHER SOURCE(S): MARPAT 116:214350
IT **120072-59-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 120072-59-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



IT **141059-14-5P 141059-19-0P 141059-22-5P**
141059-25-8P 141059-28-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as LTB4 antagonist)

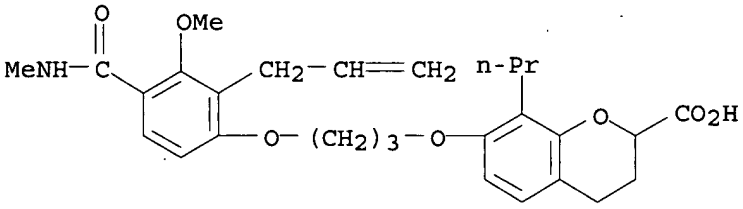
RN 141059-14-5 CAPLUS

CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[2-(cyclopropylmethyl)-3-methoxy-4-[(methylamino)carbonyl]phenoxy]propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



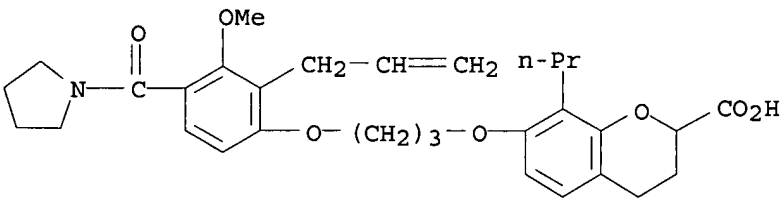
RN 141059-19-0 CAPLUS

CN 2H-1-Benzopyran-2-carboxylic acid, 3,4-dihydro-7-[3-[3-methoxy-4-[(methylamino)carbonyl]-2-(2-propenyl)phenoxy]propoxy]-8-propyl- (9CI) (CA INDEX NAME)



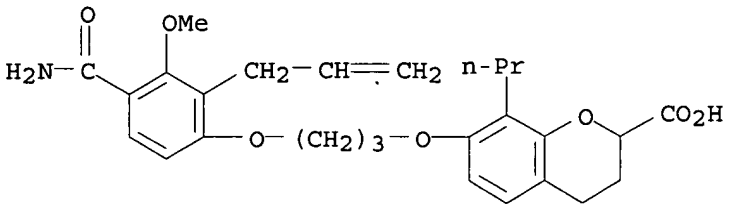
RN 141059-22-5 CAPLUS

CN 2H-1-Benzopyran-2-carboxylic acid, 3,4-dihydro-7-[3-[3-methoxy-2-(2-propenyl)-4-(1-pyrrolidinylcarbonyl)phenoxy]propoxy]-8-propyl- (9CI) (CA INDEX NAME)



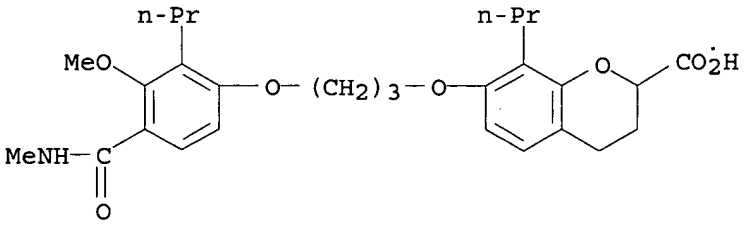
RN 141059-25-8 CAPLUS

CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[4-(aminocarbonyl)-3-methoxy-2-(2-propenyl)phenoxy]propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)

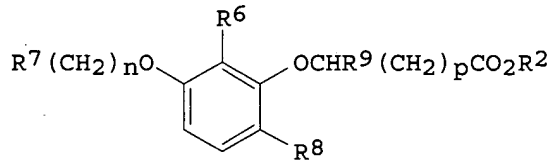


RN 141059-28-1 CAPLUS

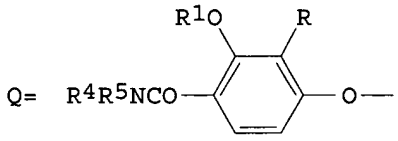
CN 2H-1-Benzopyran-2-carboxylic acid, 3,4-dihydro-7-[3-[3-methoxy-4-[(methylamino)carbonyl]-2-propylphenoxy]propoxy]-8-propyl- (9CI) (CA INDEX NAME)

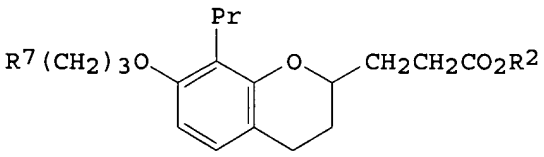


GI



I

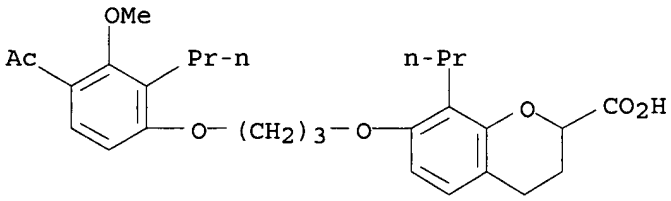




II

AB Title compds. {I; R2 = H, alkyl; R6 = alkyl; R7 = carbamoylphenoxy group Q; R = alkyl, alkenyl, alkynyl, (CH2)mR3; R1 = alkyl; R3 = cycloalkyl; R4,R5 = H, alkyl; NR4R5 = heterocyclyl; R8, R9 = H; R8R9 = CH2CH2; m = 1,2; n = 3-7; p = 0-6] were prepd. Thus, benzopyranpropanoate II (R2 = Me, R7 = iodo) (prepn. given) was condensed with QH (R = allyl, R1 = R5 = H, R4 = Me) (prepn. given) to give II (R7 = Q, R = alkyl, R4 = Me, R5 = H) (III; R2 = Me, R1 = H) which was converted in 2 steps to III (R2 = H, R1 = Me). The latter was 8.9 times as effective as 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl-2H-1-benzopyran-2-carboxylic acid in inhibition of binding of LTB4 at human neutrophils in vitro.

L4 ANSWER 35 OF 48 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:145642 CAPLUS
DOCUMENT NUMBER: 116:145642
TITLE: Induction of colitis in rats by 2,2'-azobis[2-amidinopropane] dihydrochloride
AUTHOR(S): Tamai, Hiroshi; Levin, Stuart; Gaginella, Timothy S.
CORPORATE SOURCE: Searle Res. and Dev., Skokie, IL, 60077, USA
SOURCE: Inflammation (New York, NY, United States) (1992), 16(1), 69-81
CODEN: INFLD4; ISSN: 0360-3997
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **120072-59-5**, SC-41930
RL: BIOL (Biological study)
(azobis(amidinopropane)-induced colitis prevention by)
RN 120072-59-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



AB 2,2'-Azobis[2-amidinopropane] dihydrochloride (AAPH), an azo compd. that generates free radicals in vitro, was administered intrarectally to rats. Acute mucosal injury was assessed histol. by light microscopy and biochem. by myeloperoxidase (MPO) activity. Intrarectal administration of AAPH (60, 90, and 150 mg/kg) caused erythema, edema, and histol. verifiable mucosal inflammation. MPO activity was increased 9-18-fold above the control level. The levels of thiobarbituric acid reactants and sulfhydryls were significantly increased and decreased, resp., by 90 mg/kg AAPH. Sulfasalazine, 5-aminosalicylic acid, the LTB4 receptor antagonist SC 41930, and the antioxidant glutathione prevented the inflammation. This model of mucosal inflammation may be useful in evaluating new therapeutic agents for the treatment of inflammatory bowel **disease** .

L4 ANSWER 36 OF 48 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:83676 CAPLUS
DOCUMENT NUMBER: 116:83676
TITLE: Preparation of heterocycles containing alkoxy-substituted dihydrobenzopyran-2-carboxylic acids as leukotriene B4 (LTB4) antagonists
INVENTOR(S): Djuric, Stevan Wakefield; Penning, Thomas Dale; Snyder, James Patrick
PATENT ASSIGNEE(S): Searle, G. D., and Co., USA
SOURCE: PCT Int. Appl., 90 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9117160	A1	19911114	WO 1991-US2981	19910501

W: AT, AU, BB, BG, BR, CA, CH, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MC, MG, MW, NL, NO, PL, RO, SD, SE, SU, US

RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IT, LU, ML, MR, NL, SE, SN, TD, TG

US 5073562	A	19911217	US 1990-521777	19900510
CA 2082500	AA	19911111	CA 1991-2082500	19910501
AU 9179020	A1	19911127	AU 1991-79020	19910501
AU 647487	B2	19940324		
EP 527922	A1	19930224	EP 1991-910026	19910501
EP 527922	B1	19950308		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE

JP 05507084	T2	19931014	JP 1991-509388	19910501
ES 2069295	T3	19950501	ES 1991-910026	19910501
IL 98090	A1	19950731	IL 1991-98090	19910509
ZA 9103546	A	19920729	ZA 1991-3546	19910510
US 5192782	A	19930309	US 1991-759272	19910913
US 5212198	A	19930518	US 1992-958632	19921009

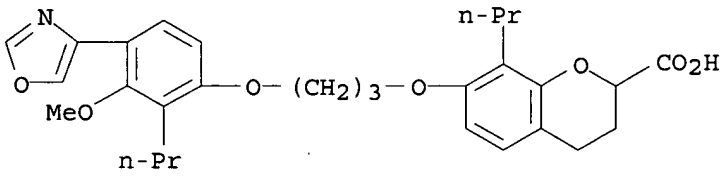
PRIORITY APPLN. INFO.: US 1990-521777 19900510
WO 1991-US2981 19910501
US 1991-759272 19910913

OTHER SOURCE(S): MARPAT 116:83676

IT **138828-24-7P 138828-27-0P 138828-28-1P**
138828-29-2P 138828-31-6P 138828-33-8P
138828-36-1P 138828-39-4P 138828-42-9P
138828-44-1P 138828-46-3P 138828-47-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as LTB4 antagonist)

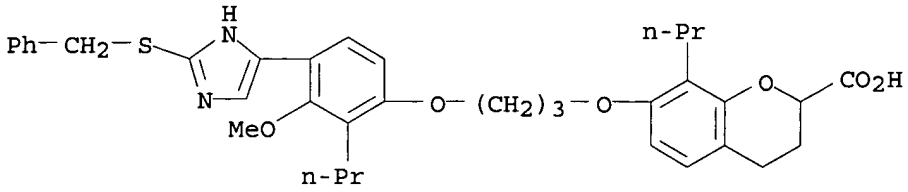
RN 138828-24-7 CAPLUS

CN 2H-1-Benzopyran-2-carboxylic acid, 3,4-dihydro-7-[3-[3-methoxy-4-(4-oxazolyl)-2-propylphenoxy]propoxy]-8-propyl- (9CI) (CA INDEX NAME)



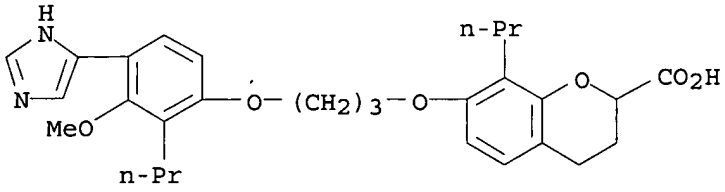
RN 138828-27-0 CAPLUS

CN 2H-1-Benzopyran-2-carboxylic acid, 3,4-dihydro-7-[3-[3-methoxy-4-[2-[(phenylmethyl)thio]-1H-imidazol-4-yl]-2-propylphenoxy]propoxy]-8-propyl- (9CI) (CA INDEX NAME)

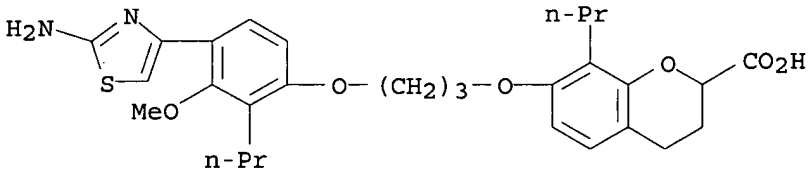


RN 138828-28-1 CAPLUS

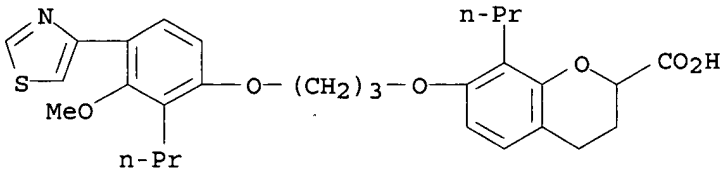
CN 2H-1-Benzopyran-2-carboxylic acid, 3,4-dihydro-7-[3-[4-(1H-imidazol-4-yl)-3-methoxy-2-propylphenoxy]propoxy]-8-propyl- (9CI) (CA INDEX NAME)



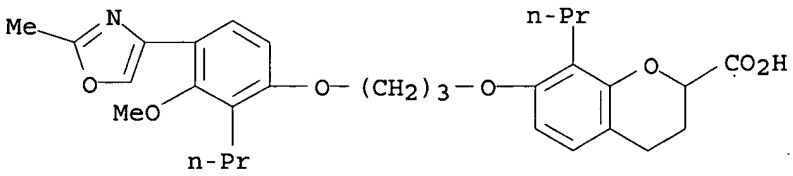
RN 138828-29-2 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[4-(2-amino-4-thiazolyl)-3-methoxy-2-propylphenoxy]propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



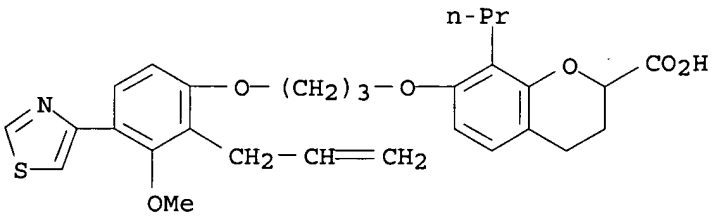
RN 138828-31-6 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 3,4-dihydro-7-[3-[3-methoxy-2-propyl-4-(4-thiazolyl)phenoxy]propoxy]-8-propyl- (9CI) (CA INDEX NAME)



RN 138828-33-8 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 3,4-dihydro-7-[3-[3-methoxy-4-(2-methyl-4-oxazolyl)-2-propylphenoxy]propoxy]-8-propyl- (9CI) (CA INDEX NAME)

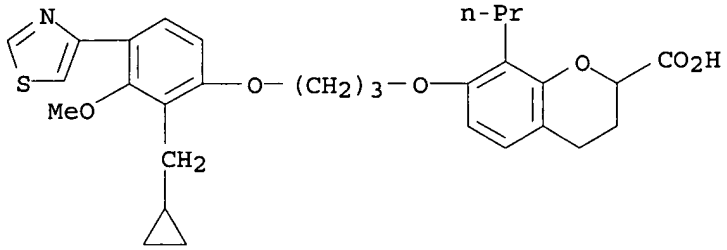


RN 138828-36-1 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 3,4-dihydro-7-[3-[3-methoxy-2-(2-propenyl)-4-(4-thiazolyl)phenoxy]propoxy]-8-propyl- (9CI) (CA INDEX NAME)

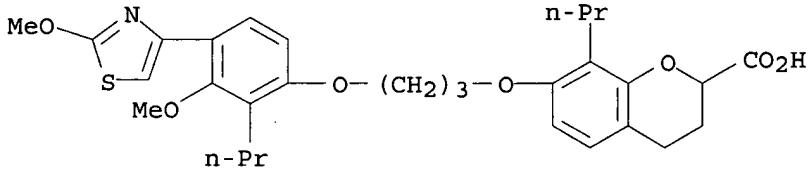


RN 138828-39-4 CAPLUS

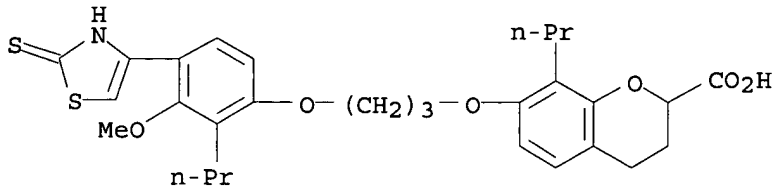
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[2-(cyclopropylmethyl)-3-methoxy-4-(4-thiazolyl)phenoxy]propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



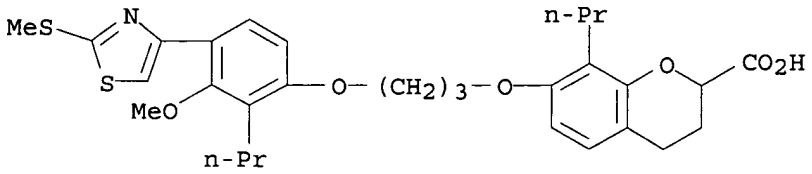
RN 138828-42-9 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 3,4-dihydro-7-[3-[3-methoxy-4-(2-methoxy-4-thiazolyl)-2-propylphenoxy]propoxy]-8-propyl- (9CI) (CA INDEX NAME)



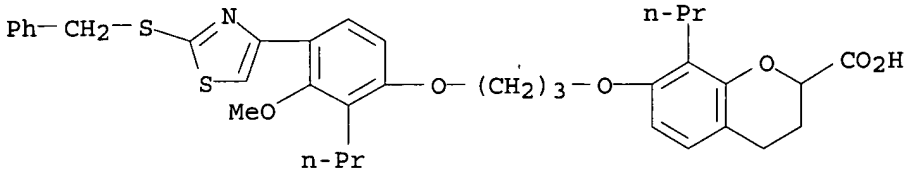
RN 138828-44-1 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[4-(2,3-dihydro-2-thioxo-4-thiazolyl)-3-methoxy-2-propylphenoxy]propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



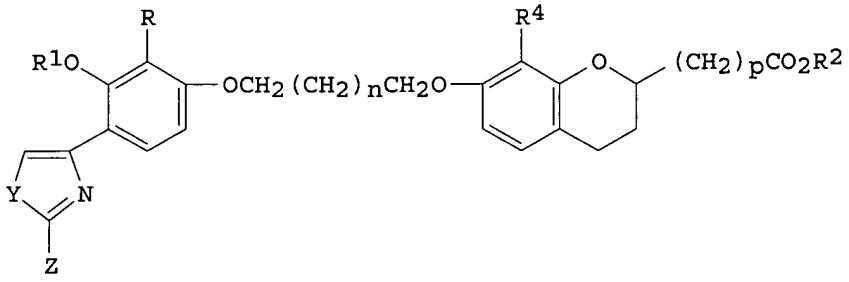
RN 138828-46-3 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 3,4-dihydro-7-[3-[3-methoxy-4-[2-(methylthio)-4-thiazolyl]-2-propylphenoxy]propoxy]-8-propyl- (9CI) (CA INDEX NAME)



RN 138828-47-4 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 3,4-dihydro-7-[3-[3-methoxy-4-[2-[(phenylmethyl)thio]-4-thiazolyl]-2-propylphenoxy]propoxy]-8-propyl- (9CI) (CA INDEX NAME)



GI



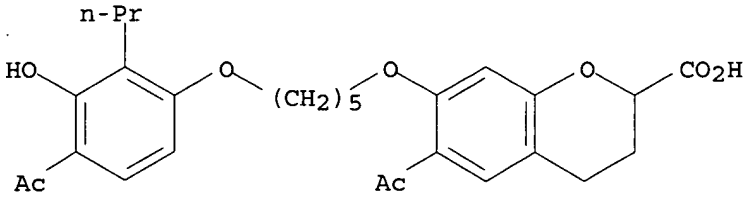
I

AB Title compds. I (R = C2-6 alkyl, C2-6 alkenyl, C2-6 alkynyl, R3(CH2)m, wherein R3 = C3-5 cycloalkyl, m = 1,2; R1 = C1-4 alkyl; R2 = H, C1-5 alkyl; R4 = C1-6 alkyl; n = 1-5; p = 0-6; Y = NH, O, S; Z = H, C1-4 alkyl, C1-4 alkoxy, R5R4N wherein R4, R5 = H, C1-4 alkyl, R6S wherein R6 = H, PhCH2, C1-4 alkyl), stereoisomers and salts thereof, are prepd. I as LTB4 antagonists are useful as antiinflammatory agents and in treatment of LTB4-mediated **conditions**. The 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl-2H-1-benzopyran-2-carboxylate (prepn. given) was converted to the 2-hydroxy-1-oxoethyl deriv. which was treated with (F3CSO2)2O to give the 2-(trifluoromethylsulfonyloxy deriv. This compd. was stirred with HCONH2 and DMF to give I (R = R4 = Pr, R1 = R2 = Me, Y = O, Z = H, n = 1, p = 0) which was stirred with LiOH to give I (R = R4 = Pr, R1 = Me, R2 = Z = H, Y = O, n = 1, p = 0) (II). II and other title compds. showed LTB4 antagonism.

L4 ANSWER 37 OF 48 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:721 CAPLUS
DOCUMENT NUMBER: 116:721
TITLE: Pheroxypentyloxy-3,4-dihydro-2H-1-benzopyran derivatives for treatment of leukotriene-induced inflammation of the intestinal mucosa
PATENT ASSIGNEE(S): Hoffmann-La Roche, F. A.-G., Switz.
SOURCE: Austrian, 20 pp.
CODEN: AUXXAK
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

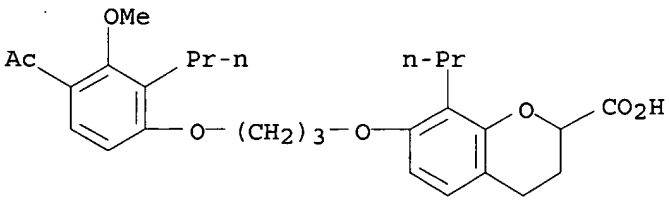
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
AT 392902	B	19910710	AT 1987-2643	19871008
AT 8702643	A	19901215		

OTHER SOURCE(S): MARPAT 116:721
IT **96566-25-5 131147-29-0 131147-29-0D**, esters
RL: BIOL (Biological study)
(leukotriene-induced intestinal mucosa inflammation treatment with)
RN 96566-25-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 6-acetyl-7-[[5-(4-acetyl-3-hydroxy-2-propylphenoxy)pentyl]oxy]-3,4-dihydro- (9CI) (CA INDEX NAME)



RN 131147-29-0 CAPLUS
RN 131147-29-0 CAPLUS
AB The title compds., esp. racemic 6-acetyl-7-[5-(4-acetyl-3-hydroxy-2-propylphenyloxy)pentyloxy]-3,4-dihydro-2H-1-benzopyran-2-carbonic acid (I), are prepd. as oral, rectal, or parenteral formulations. I at 10-100 mg/kg orally was effective against clindamycin-induced colitis in hamsters.

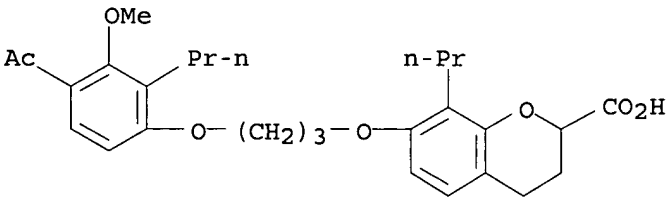
L4 ANSWER 38 OF 48 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:597978 CAPLUS
DOCUMENT NUMBER: 115:197978
TITLE: The antiinflammatory agent SC-41930 inhibits granulocyte infiltration of the rodent dermis induced by 6-trans-leukotriene B4
AUTHOR(S): Fretland, D. J.; Widomski, D. L.; Anglin, C. P.; Gaginella, T. S.
CORPORATE SOURCE: Searle Res. Dev., Skokie, IL, 60077, USA
SOURCE: Prostaglandins, Leukotrienes and Essential Fatty Acids (1991), 44(1), 61-5
CODEN: PLEAEU; ISSN: 0952-3278
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **120072-59-5**, SC-41930
RL: BIOL (Biological study)
(granulocyte infiltration stimulation by leukotriene B4 inhibition by, inflammation inhibition in relation to)
RN 120072-59-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



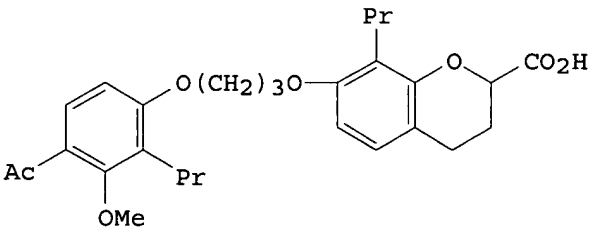
AB Granulocyte diapedesis in response to the generation of defined chemotaxins such as leukotriene B4 (LTB4), 12(R)-hydroxyeicosatetraenoic acid [12(R)-HETE], C5a, platelet activating factor and others is a hallmark of the inflammatory process that is thought to contribute to the tissue pathol. seen in a no. of **diseases**. 6-trans-LTB4 arises through the myeloperoxidase (MPO)-HETE. The intradermal (i.d.) injection of 6-trans-LTB4 induces a dose and time dependent influx of granulocytes into the guinea-pig (Hartley) dermis. When various doses of the LTB4 receptor antagonist and antiinflammatory agent, SC-41930 {7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)-propoxy]-3,4-dihydro-8-propyl-2H-1-benzopyran-2-carboxylic acid} given 30 min ahead of i.d. injection of 6-trans-LTB4 (10 .mu.g/i.d. site), granulocyte infiltration, as assessed by dermal levels of the neutrophil marker enzyme MPO was inhibited with an

ED50 value of 9.8 mg/kg in the guinea-pig. When various doses (10-25 .mu.g) 6-trans-LTB4 were injected in the mouse (CD-1) dermis, there was a dose-related increase in granulocyte accumulation at 4 h. Furthermore when mice were pretreated (-30 min) with SC-41930 (1 mg/kg) orally, the trafficking of granulocytes was inhibited ($p < .01$) as assessed by dermal MPO levels. SC-41930 orally inhibits 6-trans-LTB4-induced granulocyte accumulation in the guinea-pig more potently than against the response to 12(R)-HETE(ED50:13.4 mg/kg) but less potently than against LTB4 (ED50:0.6 mg/kg). These multiple activities may contribute to this compd.'s potential as an inflammation inhibitor.

L4 ANSWER 39 OF 48 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:549984 CAPLUS
DOCUMENT NUMBER: 115:149984
TITLE: Effect of the leukotriene B4 receptor antagonist, SC-41930, on experimental allergic encephalomyelitis (EAE) in the guinea pig
AUTHOR(S): Fretland, D. J.; Widomski, D. L.; Shone, R. L.; Levin, S.; Gaginella, T. S.
CORPORATE SOURCE: Dep. Pathol., Searle Res. and Dev., Skokie, IL, 60077, USA
SOURCE: Agents and Actions (1991), 34(1-2), 172-4
CODEN: AGACBH; ISSN: 0065-4299
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **120072-59-5**, SC-41930
RL: BIOL (Biological study)
(multiple sclerosis treatment with, allergic encephalomyelitis model in relation to)
RN 120072-59-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



GI

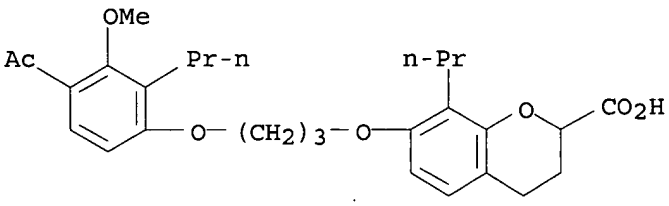


I

AB The accepted model for the human demyelinating **disease**, multiple sclerosis (MS), is exptl. allergic encephalomyelitis (EAE). The ability of SC-41930 (I) to modulate the symptoms of acute EAE was examd. in guinea pigs. Animals were pretreated with SC-41930 (20 mg/kg, i.p.) for two days followed by thrice-weekly maintenance. At day 52, a significant no. of the SC-41930-treated animals were alive as compared to EAE alone. Control animals had an increase in body wt. while EAE animals lost over 20%

(p<0.5) of their body wt. by day 18. SC-41930-treatment significantly reduced, but did not completely inhibit the cachectic response. The results indirectly implicate LTB4 in the pathogenesis of EAE. Agents that modify this model may be useful in the treatment of human MS.

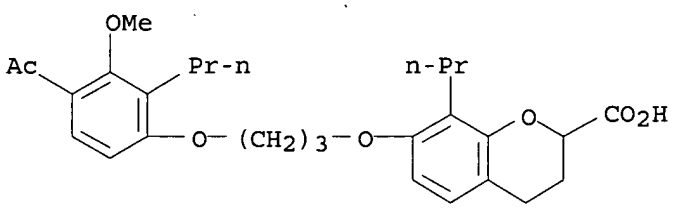
L4 ANSWER 40 OF 48 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:178176 CAPLUS
DOCUMENT NUMBER: 114:178176
TITLE: A23187-induced pulmonary gas trapping and inflammation in the guinea pig
AUTHOR(S): Stengel, Peter W.; Williams, G. D.; Silbaugh, S. A.
CORPORATE SOURCE: Lilly Res. Lab., Indianapolis, IN, 46285, USA
SOURCE: Agents and Actions (1991), 32(3-4), 270-6
CODEN: AGACBH; ISSN: 0065-4299
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **120072-59-5**, SC 41930
RL: BIOL (Biological study)
(lung obstruction and inflammation from A 23187 response to)
RN 120072-59-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



AB A brief A23187 aerosol exposure produced prolonged airway obstruction with granulocyte accumulation in conscious guinea pigs. Aminophylline, atropine, pyrilamine, salbutamol, SC-41930 (a leukotriene B4 antagonist) and WEB 2086 (a platelet-activating factor antagonist) were administered i.v. to evaluate their ability to prevent these changes. Inhaled salbutamol was also assessed. Aminophylline, atropine, and salbutamol (i.v. and aerosol) inhibited the A23187-induced pulmonary gas trapping. Pyrilamine, SC-41930 and WEB 2086 did not influence this airway-obstructive effect. Only atropine, inhaled salbutamol and SC-41930 inhibited the cell influx, while pyrilamine potentiated the inflammation. Apparently, A23187 produces a sustained bronchospasm and an intense granulocyte accumulation. The treatment agents tested differ considerably in their ability to alter A23187-induced obstruction and inflammation.

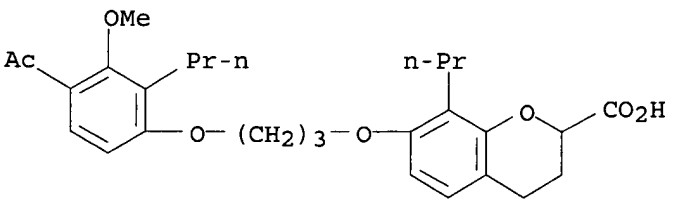
L4 ANSWER 41 OF 48 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:157171 CAPLUS
DOCUMENT NUMBER: 114:157171
TITLE: SC-41930, a leukotriene B4 receptor antagonist, inhibits 12(S)-hydroxyeicosatetraenoic acid (12(S)-HETE) binding to epidermal cells
AUTHOR(S): Kemeny, I.; Ruzicka, T.
CORPORATE SOURCE: Dep. Dermatol., Univ. Munich, Munich, 8000/2, Germany
SOURCE: Agents and Actions (1991), 32(3-4), 339-42
CODEN: AGACBH; ISSN: 0065-4299
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **120072-59-5**, SC-41930
RL: BIOL (Biological study)
(hydroxyeicosatetraenoic acid receptors antagonism by, in epidermal cells of humans)
RN 120072-59-5 CAPLUS

CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



AB SC-41930, 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)-propoxyl]-3,4-dihydro-8-propyl-2H-1-benzopyran-2-carboxylic acid, a potent leukotriene-B4 (LTB4) receptor antagonist, inhibits in vivo 12-hydroxyeicosatetraenoic acid (12-HETE)-induced neutrophil infiltration, suggesting a potential 12-HETE receptor antagonist effect, as well. Since 12-HETE is assumed to have a pathophysiol. role in inflammatory skin **diseases**, and epidermal cells possess high affinity binding sites for 12(S)-HETE, the effect of SC-41930 on 12(S)-HETE binding to the human epidermal cell line, SCL-II was studied. SC-41930 antagonized the 12(S)-HETE binding to SCL-II cells with a Ki of 480 nM. This Ki value is similar to that obtained for the inhibition of LTB4 binding to human neutrophils. Those results show that SC-41930, in addn. to its LTB4 receptor antagonist effect, exhibits 12-HETE receptor antagonist effect as well, and therefore may be of benefit in skin **diseases** with elevated 12-HETE levels.

L4 ANSWER 42 OF 48 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:35615 CAPLUS
DOCUMENT NUMBER: 114:35615
TITLE: Effect of the leukotriene B4 receptor antagonist SC-41930 on colonic inflammation in rat, guinea pig and rabbit
AUTHOR(S): Fretland, Donald J.; Widomski, Deborah; Tsai, Bie Shung; Zemaitis, Jeanne M.; Levin, Stuart; Djuric, Stevan W.; Shone, Robert L.; Gaginella, Timothy S.
CORPORATE SOURCE: Dep. Gastrointest. Dis. Res., Searle Res. and Dev., Skokie, IL, 60077, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (1990), 255(2), 572-6
CODEN: JPETAB; ISSN: 0022-3565
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **120072-59-5**, SC 41930
RL: BIOL (Biological study)
(colon inflammation prevention by, as leukotriene B4 antagonist, in inflammatory bowel **disease** model)
RN 120072-59-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



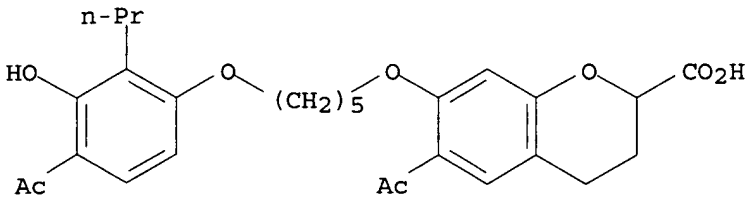
AB Inflammatory bowel **disease** is a chronic inflammatory **disorder** of the gastrointestinal tract that includes ulcerative

colitis and Crohn's **disease**. Leukotriene B4 is thought to be a prominent proinflammatory mediator in these **diseases**, in that leukotriene B4 levels are increased in the colonic mucosa of inflammatory bowel **disease** patients and there is increased polymorphonuclear leukocyte infiltration of these tissues. The efficacy of 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)-3,4-dihydro-8-propyl-2H-1-benzopyran-2-carboxylic acid (SC-41930), a potent, orally active leukotriene B4 receptor antagonist, in a model of inflammatory bowel **disease** was examd. Colonic mucosal inflammation was induced in rats, guinea pig and rabbits by rectal instillation of a dil. soln. of acetic acid. Twenty-four hours later, mucosal levels of myeloperoxidase (a marker enzyme for neutrophil infiltration) and extravasation of i.v. administered Evans blue dye (a marker of vascular disruption and increased permeability) were measured. Tissues were also evaluated histol. The animals received either SC-41930 or vehicle, intrarectally, 30 min after or 1 h before and 1 h after the acetic acid. When given 30 min after acetic acid instillation SC-41930 prevented the rise in myeloperoxidase and dye extravasation obsd. in the acetic acid inflamed tissue. The SC-41930-treated tissues were less edematous and had fewer neutrophils within the subepithelial space. Median ED (ED50) values for vascular protection were approx. 20 mg/kg for both rat and guinea pig. ED50 values for inhibition of granulocyte accumulation were 20 mg/kg for rat, 24 mg/kg for guinea pig and 30 mg/kg for rabbit. These data indicate that SC-41930 is effective locally to prevent acute colonic inflammation.

L4 ANSWER 43 OF 48 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1990:216695 CAPLUS
DOCUMENT NUMBER: 112:216695
TITLE: Preparation and formulation of phenoxyalkoxy-3,4-dihydro-2H-1-benzopyrans for therapy of allergic and inflammatory **disorders**
INVENTOR(S): Laurenzano, Anthony James; Partridge, John Joseph
PATENT ASSIGNEE(S): Hoffmann-La Roche, F., und Co. A.-G., Switz.
SOURCE: Eur. Pat. Appl., 31 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

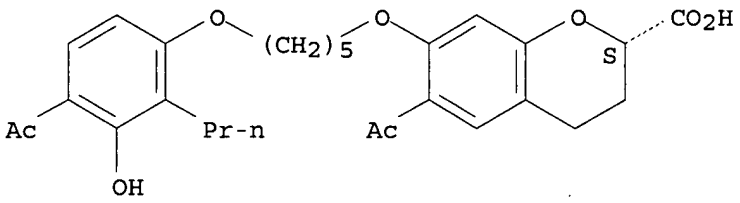
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 336068	A1	19891011	EP 1989-101886	19890203
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
DK 8900596	A	19890812	DK 1989-596	19890209
JP 01246275	A2	19891002	JP 1989-28803	19890209
ZA 8901036	A	19891025	ZA 1989-1036	19890209
AU 8929820	A1	19890817	AU 1989-29820	19890210

PRIORITY APPLN. INFO.: US 1988-154765 19880211
OTHER SOURCE(S): MARPAT 112:216695
IT **96566-25-5 96686-71-4 96686-73-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(esterification of)
RN 96566-25-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 6-acetyl-7-[[5-(4-acetyl-3-hydroxy-2-propylphenoxy)pentyl]oxy]-3,4-dihydro- (9CI) (CA INDEX NAME)



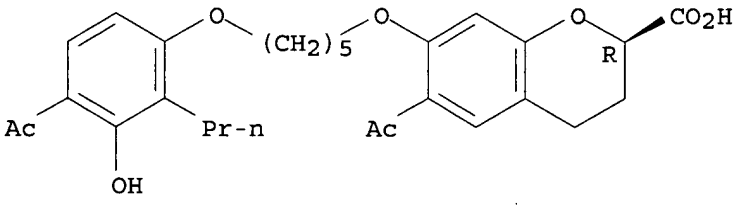
RN 96686-71-4 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 6-acetyl-7-[[5-(4-acetyl-3-hydroxy-2-propylphenoxy)pentyl]oxy]-3,4-dihydro-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 96686-73-6 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 6-acetyl-7-[[5-(4-acetyl-3-hydroxy-2-propylphenoxy)pentyl]oxy]-3,4-dihydro-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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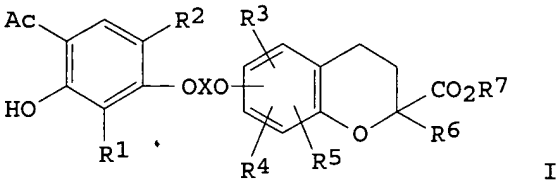
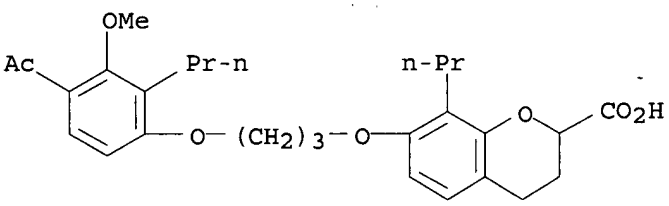


I

AB Title compds. I (R1, R6 = H, alkyl; R2 = H, halo; R3-R5 = H, acyl, alkyl provided only 1 group is acyl; R7 = higher alkyl, PhCH2; X = C3-7 alkylene) and their enantiomers were prepd. and formulated. Thus, (.+-.)-6-acetyl-7-[5-(4-acetyl-3-hydroxy-2-propylphenoxy)pentyloxy]-3,4-dihydro-2H-1-benzopyran-2-carboxylic acid (II) was esterified by 1-octanol in PhMe with p-MeC6H4SO3H.H2O catalyst under Dean-Stark **conditions** to give II n-octyl ester (III) in 75% yield. Tablets contg. III, lactose, starch, polyvinylpyrrolidone, and Mg stearate were prepd. and coated with a soln. of hydroxypropyl methylcellulose phthalate in alc.-CH2Cl2. Seven syntheses and 11 formulations are described.

L4 ANSWER 44 OF 48 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1990:111716 CAPLUS
DOCUMENT NUMBER: 112:111716
TITLE: SC-41930 inhibits neutrophil infiltration of the cavine dermis induced by 12(R)-hydroxyeicosatetraenoic acid
AUTHOR(S): Fretland, D. J.; Widomski, D. L.; Shone, R. L.; Penning, T. D.; Miyashiro, J. M.; Djuric, S. W.
CORPORATE SOURCE: Gastrointest. Dis. Res. Dep., G. D. Searle and Co., Skokie, IL, 60077, USA
SOURCE: Prostaglandins, Leukotrienes and Essential Fatty Acids (1989), 38(3), 169-72
CODEN: PLEAEU; ISSN: 0952-3278
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **120072-59-5**, SC-41930
RL: BIOL (Biological study)
(neutrophil infiltration inhibition by, psoriasis in relation to)
RN 120072-59-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



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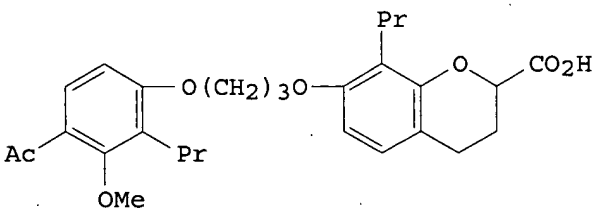
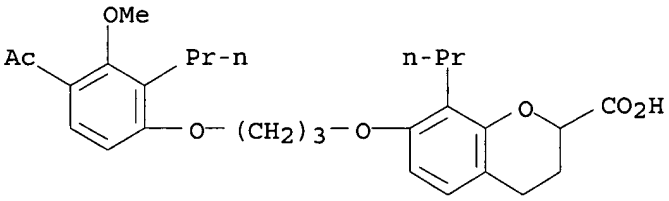


I

AB Psoriasis is a **disease** state characterized by epidermal proliferation, neutrophil infiltration, and release of the proinflammatory mediators leukotriene-B4 (LTB4) and 12(R)-hydroxyeicosatetraenoic acid [12(R)-HETE]. LTB4 and 12(R)-HETE are chemoattractant to the neutrophil, the latter approx. 1000-fold less potent. LTB4 and 12(R)-HETE are present in psoriatic scale, the latter in quantities so much greater than LTB4 that it is proposed as a primary mediator of neutrophil infiltration in psoriasis. 12(R)-HETE, synthesized in optically pure form by a new, shorter route, was injected into the cavine dermis. At a dose of 25 .mu.g per intradermal site, 12(R)-HETE was a significant chemoattractant to the neutrophil (as assessed by dermal myeloperoxidase levels). SC-41930 (I), given intragastrically, inhibited 12(R)-HETE-induced neutrophil infiltration of the cavine dermis with an ED50 value of 13.5 mg/kg. Compds. such as SC-41930 may have utility for treating human psoriasis.

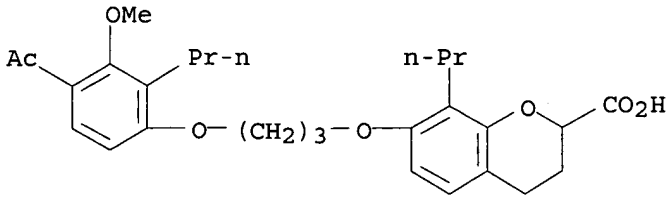
L4 ANSWER 45 OF 48 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1989:624967 CAPLUS
DOCUMENT NUMBER: 111:224967
TITLE: Effect of a leukotriene B4 receptor antagonist on leukotriene B4-induced neutrophil chemotaxis in cavine

dermis
AUTHOR(S): Fretland, D. J.; Widomski, D. L.; Zemaitis, J. M.; Djuric, S. W.; Shone, R. L.
CORPORATE SOURCE: Dep. Gastrointest. Res., G. D. Searle and Co., Skokie, IL, 60077, USA
SOURCE: Inflammation (New York, NY, United States) (1989), 13(5), 601-5
CODEN: INFLD4; ISSN: 0360-3997
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **120072-59-5**, SC 41930
RL: BIOL (Biological study)
(LTB4-induced neutrophil chemotaxis in dermis response to, inflammation inhibition in relation to)
RN 120072-59-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



AB Leukotriene B4 (LTB4) is a proinflammatory product of arachidonic acid metab. that has been implicated as a mediator in a no. of inflammatory **diseases**. When injected intradermally into the cavine, LTB4 elicites a dose-dependent immigration (chemotaxis) of neutrophils (PMNs) into the injection sites as assessed by the presence of a neutrophil marker enzyme myeloperoxidase. SC-41930, a potent LTB4 receptor antagonist inhibited the chemotactic actions of LTB4 when coadministered into the dermal site and when given i.v. or orally with ED50 values of 200 ng, 0.5 mg/kg, and 0.6 mg/kg resp. This compd. may well have application in **disease** states, such as inflammatory bowel **disease** and psoriasis, where LTB4 is implicated as a proinflammatory mediator.

L4 ANSWER 46 OF 48 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1989:433445 CAPLUS
DOCUMENT NUMBER: 111:33445
TITLE: The effect of leukotriene-B4 receptor antagonist, SC-41930, on acetic acid-induced colonic inflammation
AUTHOR(S): Fretland, D. J.; Levin, S.; Tsai, B. S.; Djuric, S. W.; Widomski, D. L.; Zemaitis, J. M.; Shone, R. L.; Bauer, R. F.
CORPORATE SOURCE: Dep. Gastrointest. Dis. Res., G. D. Searle and Co., Skokie, IL, 60077, USA
SOURCE: Agents and Actions (1989), 27(3-4), 395-7
CODEN: AGACBH; ISSN: 0065-4299
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **120072-59-5**, SC 41930
RL: BIOL (Biological study)
(intestinal inflammation therapy with, as LTB4 receptor antagonist)
RN 120072-59-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



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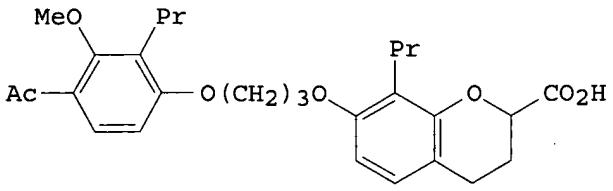


I

AB SC 41930 (I) is a potent in vitro LTB4 receptor antagonist. LTB4 levels are elevated in colonic tissue of inflammatory bowel **disease** (IBD) patients, which may account for the high degree of neutrophil (PMN) infiltration. The guinea pig acetic acid-induced colonic inflammation model has characteristics of IBD including PMN infiltration, edema, ulceration and necrosis. The model was used to evaluate the effect of SC-41930. SC-41930 was given orally, 30 min before and after intrarectal administration of 3% acetic acid. The PMN marker enzyme, myeloperoxidase, was measured along with histol. evaluation to assess inflammation. Both parameters showed significantly less inflammation in SC-41930 treated animals with an oral ED50 of 20 mg/kg. These study results indicate a role for LTB4 in colonic inflammation and that an LTB4 receptor antagonist may be beneficial for treatment of IBD.

L4 ANSWER 47 OF 48 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1989:199191 CAPLUS
DOCUMENT NUMBER: 110:199191
TITLE: Preparation of 6-acetyl-7-[5-(4-acetyl-3-hydroxy-2-propylphenoxy)pentyloxy]-3,4-dihydro-2H-1-benzopyran-2-carboxylates and antiinflammatory pharmaceuticals containing them
INVENTOR(S): Gaginella, Timothy Samuel; Welton, Ann Frances; Will, Peter Graig
PATENT ASSIGNEE(S): Hoffmann-La Roche, F., und Co. A.-G., Switz.
SOURCE: Eur. Pat. Appl., 29 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 256532	A1	19880224	EP 1987-111781	19870813
EP 256532	B1	19920520		
R: BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
ZA 8705319	A	19880427	ZA 1987-5319	19870720
IL 83533	A1	19911121	IL 1987-83533	19870813
AU 8777140	A1	19880218	AU 1987-77140	19870814
AU 607931	B2	19910321		
JP 63048216	A2	19880229	JP 1987-201953	19870814
HU 46845	A2	19881228	HU 1987-3669	19870814

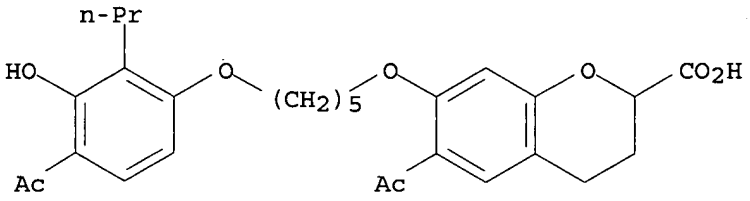
HU 203471	B	19910828			
CA 1303508	A1	19920616	CA 1987-544521	19870814	
US 5112856	A	19920512	US 1990-569241	19900816	
PRIORITY APPLN. INFO.:			US 1986-897450	19860815	
			US 1989-315014	19890224	

OTHER SOURCE(S): MARPAT 110:199191

IT **96565-55-8 96566-25-5**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceuticals contg., for treatment of enteritis)

RN 96565-55-8 CAPLUS

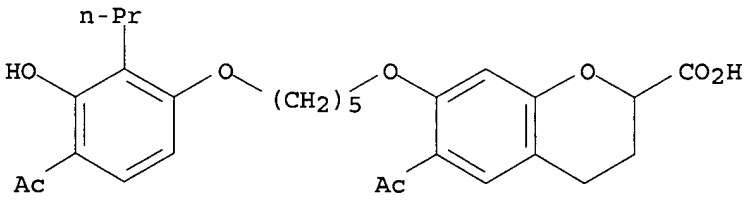
CN 2H-1-Benzopyran-2-carboxylic acid, 6-acetyl-7-[[5-(4-acetyl-3-hydroxy-2-propylphenoxy)pentyl]oxy]-3,4-dihydro-, monosodium salt (9CI) (CA INDEX NAME)



● Na

RN 96566-25-5 CAPLUS

CN 2H-1-Benzopyran-2-carboxylic acid, 6-acetyl-7-[[5-(4-acetyl-3-hydroxy-2-propylphenoxy)pentyl]oxy]-3,4-dihydro- (9CI) (CA INDEX NAME)



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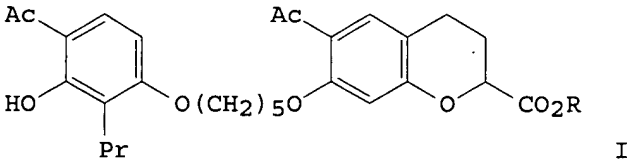


I

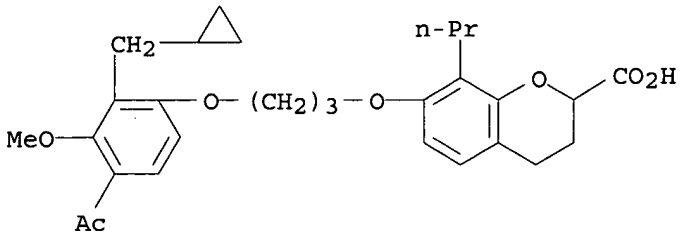
AB The title dihydrobenzopyran derivs. (I; R = H, lower alkyl), their enantiomeric forms, or their salts are inflammation inhibitors for enteritis and other forms of inflammation of the intestinal mucosa assocd. with the presence of leukotriene. A mixt. of 20.2 g Me (.+-.)-6-acetyl-7-(5-bromopentyloxy)-3,4-dihydro-2H-1-benzopyran-2-carboxylate and 11.0 g 2,4-dihydroxy-3-propylacetophenone were treated with 25.4 g K2CO3 in 436 mL dry Me2CO and 218 mL DMF for 5.5 h under reflux to give (.+-.)-I (R = Me) in 96.8% yield. Clindamycin-induced colitis in hamsters was characterized by edema, bleeding and stagnating blood flow, necrosis and mucosal erosions in the cecum and to a lesser

extend in the colon. This **condition** was improved when the animals were treated with 100 mg/kg (.+-.)-I (R = H) and the hazard ratio (survival rate of treated vs. nontreated controls) was 64.0. Tablets contained (.+-.)-I (R = H) 100, lactose 30, preglatinized starch 4, microcryst. cellulose 20, modified starch 5, and Mg stearate 1 mg.

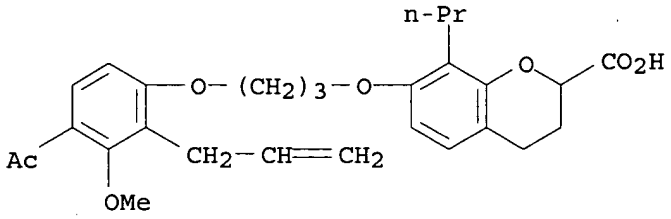
L4 ANSWER 48 OF 48 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1989:173088 CAPLUS
DOCUMENT NUMBER: 110:173088
TITLE: Preparation of alkoxy-substituted dihydrobenzopyran-2-carboxylates and analogs as antiinflammatory agents
INVENTOR(S): Djuric, Stevan Wakefield; Shone, Robert Larry; Yu, Stella Siu Tzyy
PATENT ASSIGNEE(S): Searle, G. D., and Co., USA
SOURCE: Eur. Pat. Appl., 56 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 292977	A1	19881130	EP 1988-108449	19880527
EP 292977	B1	19910904		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, NL, SE				
US 4889871	A	19891226	US 1988-188708	19880512
NO 8802317	A	19881130	NO 1988-2317	19880526
NO 171063	B	19921012		
NO 171063	C	19930120		
AU 8816681	A1	19881201	AU 1988-16681	19880526
AU 611153	B2	19910606		
IL 86502	A1	19940731	IL 1988-86502	19880526
CA 1337660	A1	19951128	CA 1988-567806	19880526
DK 8802901	A	19881130	DK 1988-2901	19880527
FI 8802505	A	19881130	FI 1988-2505	19880527
JP 01038045	A2	19890208	JP 1988-130037	19880527
JP 2758902	B2	19980528		
ZA 8803820	A	19890726	ZA 1988-3820	19880527
AT 66917	E	19910915	AT 1988-108449	19880527
ES 2051796	T3	19940701	ES 1988-108449	19880527

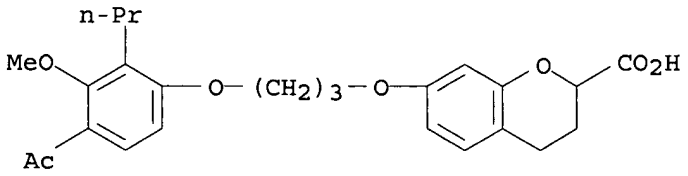
PRIORITY APPLN. INFO.: US 1987-57136 19870529
US 1988-188708 19880512
EP 1988-108449 19880527
OTHER SOURCE(S): CASREACT 110:173088; MARPAT 110:173088
IT **120072-38-0P 120072-40-4P 120072-41-5P**
120072-50-6P 120072-54-0P 120072-56-2P
120072-59-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as antiinflammatory agent)
RN 120072-38-0 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[4-acetyl-2-(cyclopropylmethyl)-3-methoxyphenoxy]propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



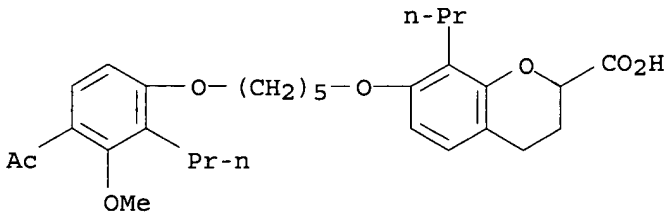
RN 120072-40-4 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-[4-acetyl-3-methoxy-2-(2-propenyl)phenoxy]propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



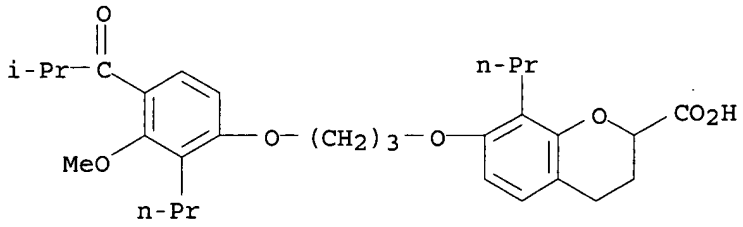
RN 120072-41-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro- (9CI) (CA INDEX NAME)



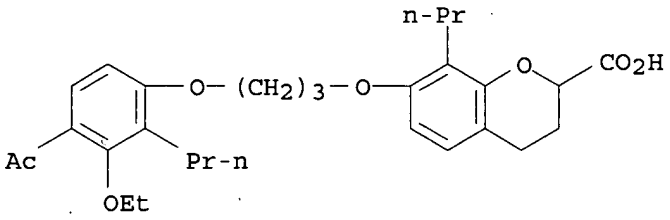
RN 120072-50-6 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[[5-(4-acetyl-3-methoxy-2-propylphenoxy)pentyl]oxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



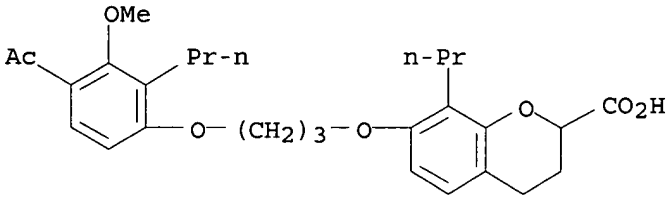
RN 120072-54-0 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 3,4-dihydro-7-[3-[3-methoxy-4-(2-methyl-1-oxopropyl)-2-propylphenoxy]propoxy]-8-propyl- (9CI) (CA INDEX NAME)



RN 120072-56-2 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-3-ethoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



RN 120072-59-5 CAPLUS
CN 2H-1-Benzopyran-2-carboxylic acid, 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl- (9CI) (CA INDEX NAME)



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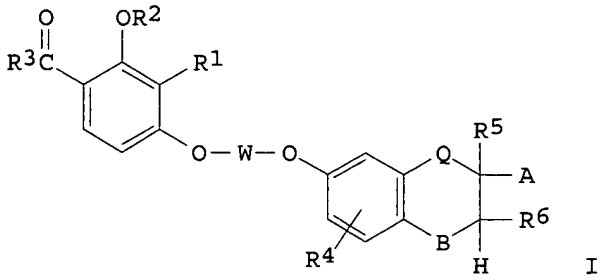
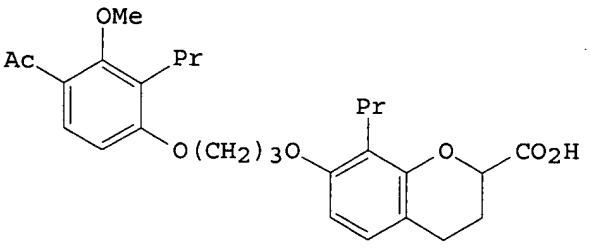


I



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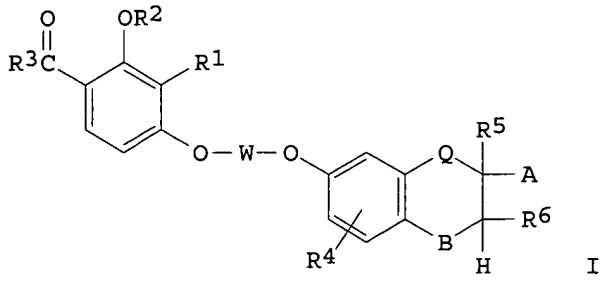

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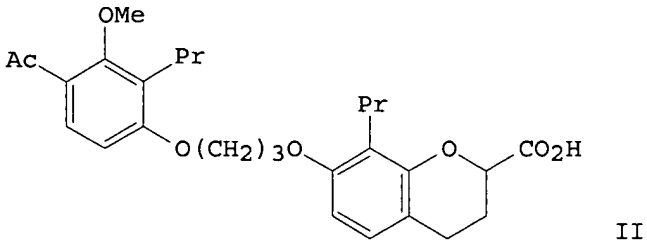

II

AB Title compds. I [R1 = C2-6 alkyl, alkenyl, or alkynyl, (CH2)nR; n = 1,2; R = C3-5 cycloalkyl; R2 = Me, Et; R3 = C1-5 alkyl; W = (CH2)x; C3-7 alkenylene or alkynylene, cyclopentanediyl; x = 2-7; R4 = H, C2-5 alkyl, alkenyl, or alkynyl; Q = O, CH2; B = CH2, CO, CHOH; R5 = H, C1-6 alkyl, C2-4 alkanoyl, CO2H, alkoxycarbonyl; (CH2)yCO2R8; R5R6 = bond; A = ZCO2R7, ZCONR9R10; Z = bond, C.ltoreq.6 alkylene or alkenylene; R7, R8 = H, C1-6 alkyl; y = 0-4; R9, R10 = H, C1-6 alkyl, C1-6 cycloalkyl; NR9R10 = heterocyclyl] were prepd. as antiinflammatory agents. Me 7-[3-(4-acetyl-3-hydroxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl-2H-1-benzopyran-2-carboxylate underwent etherification by MeI and K2CO3 in Me2CO, followed by sapon. with LiOH in aq. MeOH, to give (phenoxypropoxy)dihydrobenzopyrancarboxylic acid II. Compared to its prior art hydroxy analog II was 5-fold more potent as an LTB4 antagonist and over 10-fold less potent as an LTD4 antagonist.

=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	356.50	496.99

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-49.56	-49.56

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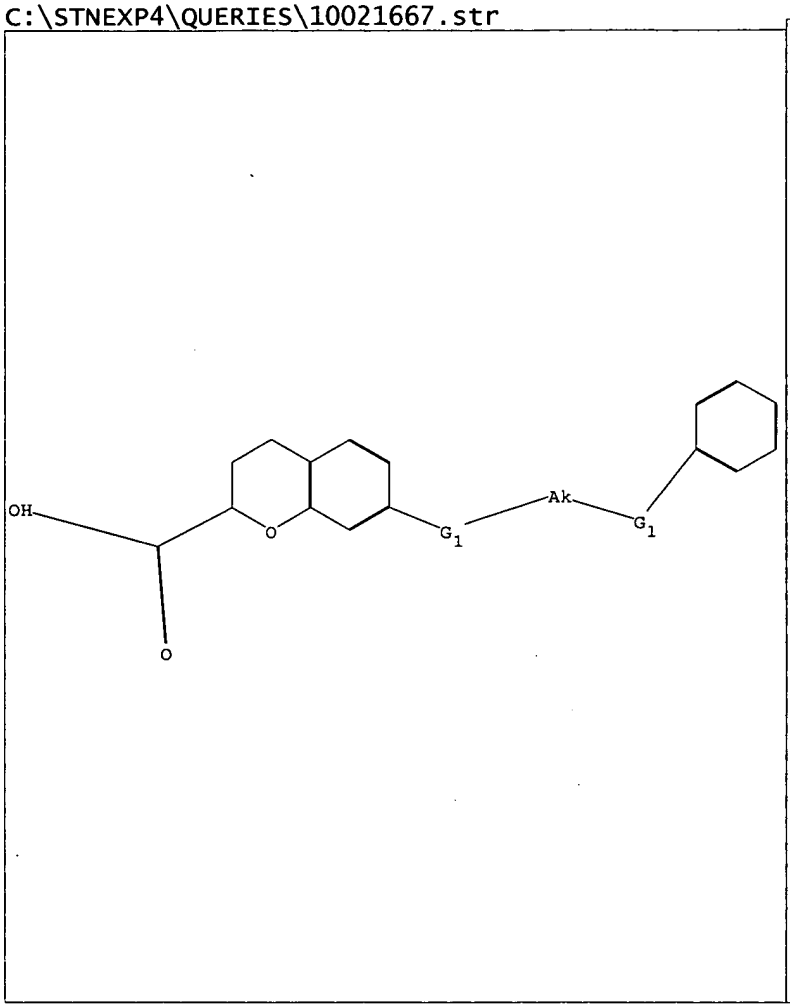

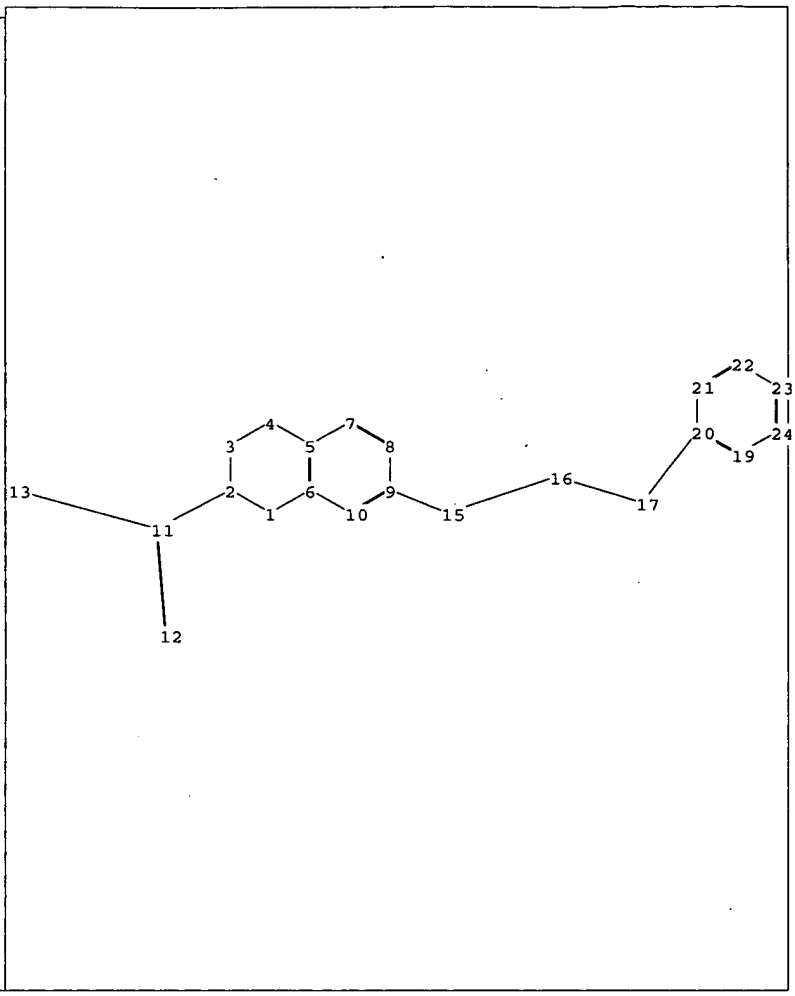

chain nodes :
11 12 13 15 16 17
ring nodes :
1 2 3 4 5 6 7 8 9 10 19 20 21 22 23 24
chain bonds :
2-11 9-15 11-12 11-13 15-16 16-17 17-20
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-10 7-8 8-9 9-10 19-20 19-24 20-21 21-22 22-23
23-24
exact/norm bonds :
1-2 1-6 2-3 3-4 4-5 9-15 15-16 16-17 17-20
exact bonds :
2-11
normalized bonds :
5-6 5-7 6-10 7-8 8-9 9-10 11-12 11-13 19-20 19-24 20-21 21-22 22-23 23-24

G1:C,O,S,N

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:CLASS
12:CLASS 13:CLASS 15:CLASS 16:CLASS 17:CLASS 19:Atom 20:Atom 21:Atom 22:Atom
23:Atom 24:Atom

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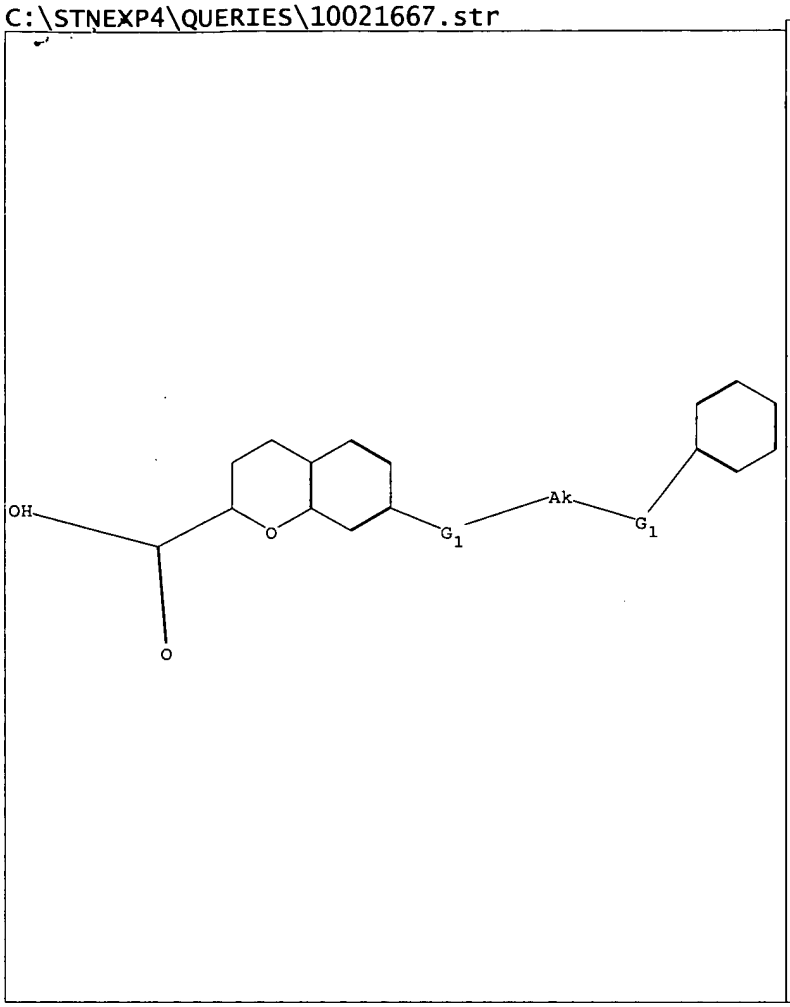

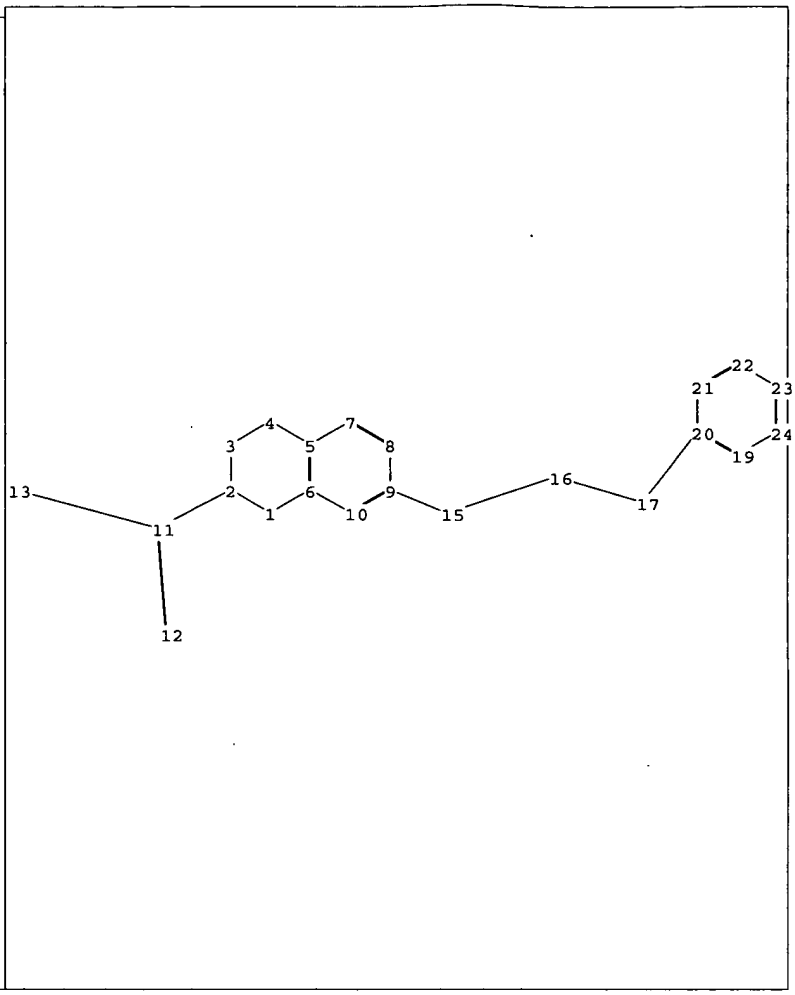

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23:Atom 24:Atom

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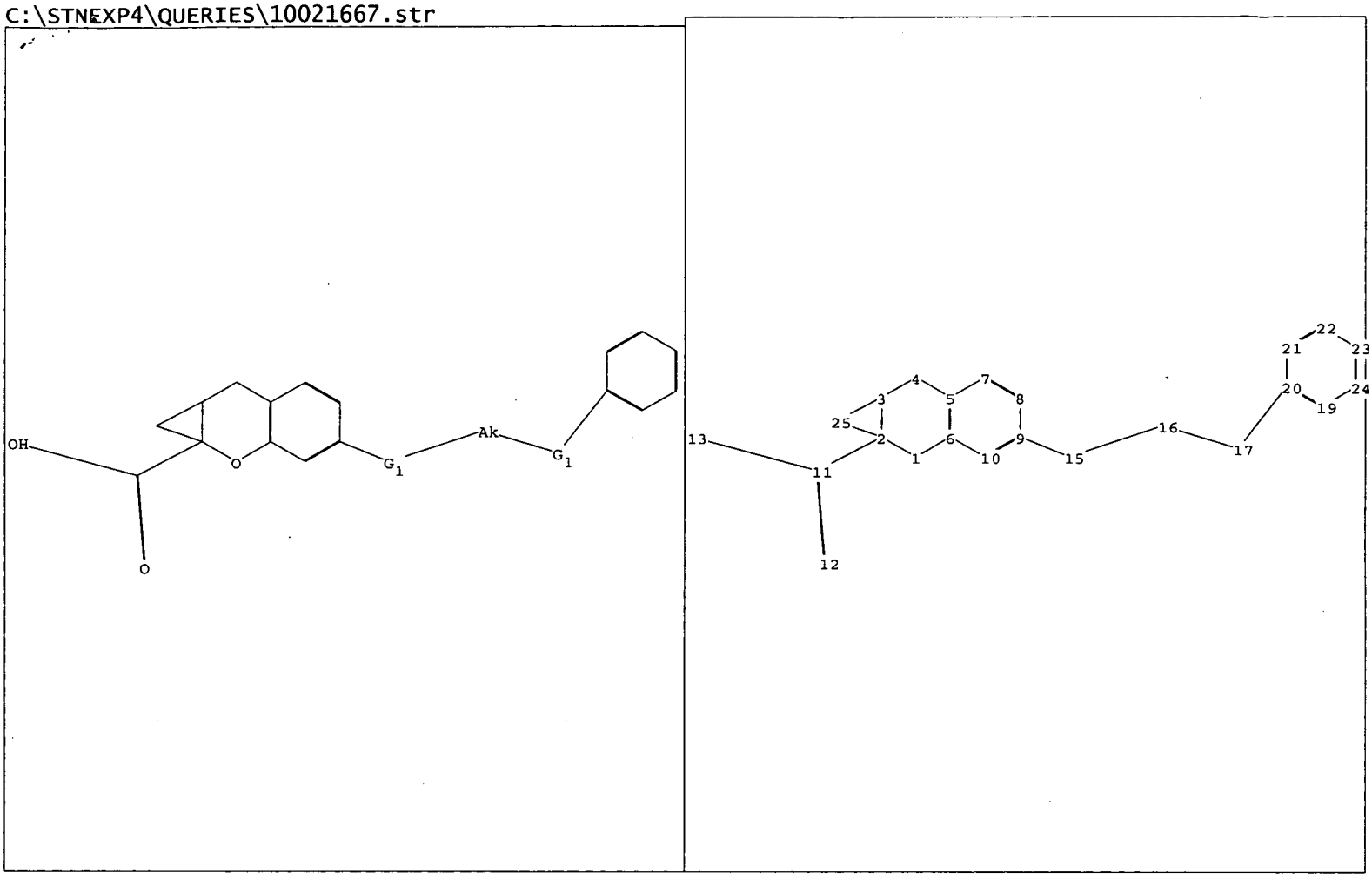

chain nodes :
11 12 13 15 16 17
ring nodes :
1 2 3 4 5 6 7 8 9 10 19 20 21 22 23 24 25
chain bonds :
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23:Atom 24:Atom 25:Atom